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Señor

DIRECTOR DIVISIÓN DE NUEVAS CREACIONES

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

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REF: Expediente No. **08 070803**– solicitud de patente de invención a favor de **COLGATE-PALMOLIVE COMPANY** Título **COMPOSICIONES ORALES MEJORADAS QUE COMPRENDEN AGENTES DE CITRATO DE ZINC**

RECURSO DE REPOSICIÓN

JUAN PABLO CADENA SARMIENTO, portador de la tarjeta profesional No. 57.492 del C.S.J., obrando como apoderado de la sociedad solicitante, manifiesto a usted que debidamente notificado de la Resolución No. 7912 del 28 de Febrero de 2013, interpongo contra ella en debido término, **RECURSO DE REPOSICIÓN**, para que sea revocada en su totalidad, y en su lugar se conceda el Privilegio de Patente, para el objeto de la solicitud en referencia.

Respaldo el RECURSO en los siguientes

HECHOS

1. La resolución arriba citada No. 7912 niega el Privilegio exclusivo de Patente de Invención para el objeto de la solicitud de la referencia, considerando que el capítulo reivindicatorio carece de nivel inventivo. Lo anterior, de acuerdo con las siguientes consideraciones.

i. Determinación del Estado de la Técnica

Consultadas las fuentes de información con que se cuenta se encontraron los siguientes documentos, que anticipan el objeto de esta solicitud.

No	Documento	Título	Fecha de publicación
D1	US 5240697	Desensitizing anti-tartar dentifricen	31/Agosto/1993
D2	US6592852	Zinc citrate beads in oral compositions	15/Julio/2003

Considera el examinador que la presente invención no cumple con el requisito de nivel inventivo, ya que su juicio la invención se considera obvia en vista de D1 y D2.

RESUELVE

ARTÍCULO PRIMERO: Denegar la patente de invención a la creación titulada **"COMPOSICIONES ORALES MEJORADAS QUE COMPRENDEN AGENTES DE CITRATO DE ZINC."**

FUNDAMENTOS

Como primera medida nos permitimos presentar un nuevo pliego reivindicatorio compuesto por nueve (9) reivindicaciones, en donde no se amplía la materia inicialmente divulgada y que encuentra entero sustento en la descripción. En este sentido, el pliego reivindicatorio en mención ha sido modificado con el fin de, (i) especificar la inclusión de un agente desensibilizador correspondiente a nitrato de potasio, en lugar de citrato de potasio, lo cual encuentra pleno sustento en la página 11 de la descripción presentada a su Despacho, e (ii) incluir como componente esencial un agente de flúor seleccionado de un grupo específico, lo cual se encuentra sustentado por la página 27 de la descripción.

De esta manera, la composición oral anti-placa y desensibilizadora objeto de la presente invención comprende los siguientes componentes,

- (i) Un agente de citrato de zinc;
- (ii) Un agente de nitrato de potasio;

- (iii) Un agente de flúor seleccionado del grupo que consiste de fluoruro de sodio, fluoruro de potasio, monofluorofosfato de sodio, fluorosilicato de sodio, fluoruro de amonio, fluoruro de amina y fluoruro de estaño;
- (iv) Un copolímero de anhídrido maleico y éter de polivinil metilo; y
- (v) Un polifosfato.

Teniendo en cuenta lo anterior, consideramos que ninguna de las referencias D1 y D2 brinda enseñanzas o sugerencias que permitan al normalmente versado en la materia llevar a cabo una selección específica de componentes para combinarlos en una misma composición.

Al respecto, cabe señalar que la presente invención da solución al problema técnico derivado de la necesidad de composiciones para el cuidado oral que reduzcan de manera efectiva el desarrollo o la progresión de placa y sarro en la cavidad oral, que además proporcionen beneficios orales tales como reducción de la sensibilidad dentinal, control de la caries y prevención de la inflamación de las encías.

Así, para dicho fin la presente invención brinda una composición oral con efectos anti-placa, que además es desensibilizadora, caracterizada porque comprende citrato de zinc, nitrato de potasio, un agente de flúor, un copolímero de anhídrido maleico y éter de polivinil metilo, y un polifosfato.

En este orden de ideas, la composición oral reivindicada brinda los siguientes beneficios:

- (i) Beneficios antibacterianos, anti-gingivitis, anti-placa, anti-sarro y de control del mal olor, debidos al citrato de zinc,
- (ii) Beneficios desensibilizadores, debidos a la presencia de nitrato de potasio,
- (iii) Beneficios anti-caries y/o anti-sarro, debidos al agente de flúor,
- (iv) Beneficio adicional de inhibición del sarro debido a la presencia de polifosfato,
- (v) Beneficios de disminución de la astringencia de la composición por formación de un complejo entre el compuesto polifosfato y los iones zinc,

- (vi) Beneficio potenciador de la eficacia de los agentes antibacterianos y anti-sarro debido a la inclusión de copolímero de anhídrido maleico y éter de polivinil metilo, y
- (vii) Beneficios adicionales de disminución de la astringencia debido a la inclusión de copolímero de anhídrido maleico y éter de polivinil metilo que forma complejos con el zinc y el compuesto polifosfato.

los cuales son exclusivamente debidos a la adecuada combinación de agentes activos.

Ahora bien, deseamos incluir datos experimentales adicionales que evidencian los beneficios técnicos adicionales derivados de la combinación específica de agentes comprendidos por la presente invención.

En este sentido se ha realizado un estudio comparativo, en términos de Absorción de fluoruro en el esmalte dental/Reducción de solubilidad del esmalte, entre la mezcla específica de tres de los ingredientes que componen la composición acá reivindicada y una composición estándar USP que comprende iones fluoruro en una concentración de 1500 ppm, con el fin de evidenciar la biodisponibilidad del ión fluoruro como agente anti-caries en la combinación específica de monofluorofosfato de sodio, nitrato de potasio y citrato de zinc. Al respecto, se obtuvieron los siguientes resultados,

Composición	Absorción F ⁻ en esmalte (ppm)	Reducción solubilidad esmalte (ppm)
Control negativo: "Winterfresh" 0 ppm F; Placebo	1.3 ± 2.7	1.0 ± 2.6
Invención: Fórmula anti-gingivitis: 2% citrato de zinc; 5% nitrato de potasio; 1500 ppm F ⁻ (1,14% NaMFP).	20.7 ± 4.9	26.4 ± 4.7
Estándar de referencia USP: Dentífrico de sílice: 1500 ppm F ⁻ como NaMFP	21.9 ± 4.2	25.8 ± 5.2

De esta manera, se demostró que en presencia de nitrato de potasio y citrato de zinc, el monofluorofosfato de sodio mantiene los mismos niveles de biodisponibilidad que se obtienen al aplicar la fuente de flúor como agente individual, lo cual es un claro indicio de

que los demás ingredientes activos de la formulación no afectan de manera negativa la actividad del agente de flúor.

Así las cosas, la presente invención incluye como parte de sus beneficios un mantenimiento de la biodisponibilidad de los iones fluoruro a pesar de la inclusión de la fuente de dichos iones como parte de una composición que incluye un agente desensibilizador (nitrado de potasio) y un agente anti-gingivitis y anti-placa (citrato de zinc).

Ahora bien, considerando la petición del examinador encargado del análisis del presente expediente relacionada con la inclusión de evidencia debidamente sustentada en ensayos comparativos de la composición reivindicada con el arte previo, nos permitimos incluir junto al presente memorial los anexos 1 y 2, los cuales corresponden a estudios clínicos dirigidos a evidenciar la eficacia de la composición objeto de la presente invención en comparación con composiciones comercialmente disponibles, en los siguientes aspectos,

- 1) Eficacia comparativa de una composición que contiene citrato de zinc, nitrato de potasio y monofluorofosfato de sodio (invención) y un dentífrico comercial que contiene 1500 ppm de fluoruro como monofluorofosfato de sodio en el **control de la placa y la gingivitis**.

En este sentido, se llevó a cabo un ensayo clínico doble-ciego, en grupo paralelo, de seis meses de duración sobre población adulta, en donde, se realizó un examen oral preliminar a cada uno de los sujetos participantes, y se asignó a cada uno un dentífrico con el cual debían cepillarse dos veces al día, con el fin de llevar a cabo posteriores exámenes sobre la cavidad oral, en términos de placa y gingivitis, tres y seis meses después del inicio del estudio para así registrar el efecto de la formulación usada.

De esta manera, entre los sujetos que completaron el estudio, es decir, aquellos que cumplieron con los seis meses de aplicación del producto asignado, se encontró que la composición que contiene 2.0% de citrato de zinc, 5.0% de nitrato de potasio y 15000 ppm de fluoruro proporciona una reducción estadísticamente significativa de la placa y la gingivitis en relación con un dentífrico comercialmente disponible que contiene únicamente fluoruro (control), en el periodo evaluado.

- 2) Eficacia de un dentífrico que contiene nitrato de potasio y monofluorofosfato de sodio (invención) y de uno comercialmente disponible (sensodyne total care F) en la **reducción de la hipersensibilidad dentinal**.

Se llevó a cabo un estudio clínico independiente, doble ciego, con una duración de ocho semanas para determinar la eficacia de una composición que comprende nitrato de potasio y monofluorofosfato de sodio en una base de sílice de bajo RDA y el dentífrico comercializado bajo el nombre Sensodyne Total Care F (control), en términos del efecto de los mismos sobre la hipersensibilidad dentinal.

Para dicho fin se seleccionaron sujetos, entre hombres y mujeres, adultos que reportaron sensibilidad dental clasificada en 2 o 3 (Sonda Yeaple) entre 10 y 50 gramos de fuerza, y una sensibilidad a chorro de aire clasificada en 2 o 3 (Escala de sensibilidad Schiff Cold).

De esta manera, los resultados permitieron concluir que el producto que comprende nitrato de potasio y monofluorofosfato de sodio proporciona una reducción significativa de la hipersensibilidad dentinal cuando es usada durante un periodo de ocho semanas, en donde, el control de dicha sensibilidad no difiere significativamente de los resultados alcanzados con el producto comercial empleado como control.

Así las cosas, la invención contempla la inclusión de una serie de características esenciales para la solución del problema técnico propuesto, las cuales **solo** derivan los beneficios listados mediante la **combinación específica** de agentes ya mencionada.

Ahora bien, la referencia **D1 (US5240697)** revela composiciones anti-sarro que comprenden una cantidad efectiva de pirofosfato de potasio como agente anti-sarro, una sal de potasio como agente desensibilizante que incluye nitrato de potasio, citrato de potasio, oxalato de potasio o una mezcla de los mismos, y un estabilizante polimérico de pirofosfato. De esta manera, aunque D1 menciona, un copolímero de anhídrido maleico y éter de polivinil metilo, no lo incluye como un ingrediente esencial sino que lo menciona como parte de una de las modalidades de la invención, sumado a lo anterior el hecho de que D1 no contempla de ninguna manera citrato de zinc como parte de la composición, tal como lo reconoció el señor Examinador.

Por su parte, la referencia **D2 (US6592852)** corresponde a un producto anti-sarro que se compone de perlas de una sal de zinc y una goma contenidas en una matriz acuosa, como parte de un producto base que se compone de colorante, abrasivos, humectantes, entre otros agentes. Así, D2 no contempla la adición específica de nitrato de potasio, un agente de flúor, un copolímero de anhídrido maleico y éter de polivinil metilo, y un polifosfato a una composición que incluye citrato de zinc, a diferencia de la presente invención.

Además, ninguna de las referencias en mención enseña, ni sugieren, que la combinación de un agente de flúor con un agente desensibilizante y un agente anti-gingivitis específicos permite la estabilidad y adecuada liberación de los iones fluoruro, y por tanto, **no** afecta la biodisponibilidad del mismo sobre la cavidad oral.

De esta manera, tal como se expuso en el listado de beneficios, la presente invención contempla una serie efectos benéficos al comprender una combinación muy específica de agentes que al ser parte de una misma composición generan una mejora sustancial de la salud oral, en comparación con las composiciones conocidas en el arte previo.

La combinación específica contemplada por la presente invención, no se encuentra revelada, ni sugerida, por ninguna de las referencias D1 o D2, pues las mismas, a pesar de contener uno o más de los agentes de la composición acá reivindicada, son silenciosas frente a la viabilidad de la combinación de los ingredientes acá reivindicados, y por tanto, no exponen en su contenido una sugerencia explícita de los efectos benéficos derivados de incluir una combinación de citrato de zinc, nitrato de potasio, un agente de flúor, un copolímero de anhídrido maleico y éter de polivinil metilo, y un polifosfato.

Por tanto, consideramos que el normalmente versado en la materia no encontraría ninguna motivación para incluir citrato de zinc a una composición que contiene nitrato de potasio como agente desensibilizante sumado a un polifosfato como agente anti-sarro, pues consideraría suficiente el efecto de cada agente por separado para generar una mejora en la salud oral, al saber que al igual que el polifosfato, el citrato de zinc actúa como agente anti-sarro, y por tanto no tendría sentido alguno incluir dos agentes con el mismo efecto, más aun al desconocer por completo si la combinación de dichos agentes daría como resultado una formulación estable.

Además, a pesar de centrarse en composiciones para el control de sarro, tanto la referencia D1 como la referencia D2, abordan dicho problema técnico por vías diferentes pues, para una es ideal emplear un agente polifosfato como agente anti-sarro, mientras que para la otra es ideal el citrato de zinc en perlas.

Por otra parte, ninguna de las referencias en cuestión considera como agente esencial el copolímero de anhídrido maleico y éter de polivinil metilo, como un agente potenciador de la actividad anti-sarro y antibacterial, por lo que en definitiva la combinación de las enseñanzas de tales referencias no permitiría al normalmente versado en la materia llegar a las enseñanzas de la presente invención.

De esta manera, las referencias D1 y D2 en combinación fallan en enseñar, o sugerir, los siguientes aspectos esenciales para la presente invención,

- Que la adición de citrato de zinc sobre la composición descrita por D1 no altere la estabilidad y compatibilidad de la composición final,
- Que la inclusión del copolímero de anhídrido maleico y éter de polivinil metilo permita potenciar la actividad anti-sarro y antibacterial,
- Que la combinación de un agente de flúor con un agente desensibilizante (nitrato de potasio) y un agente anti-gingivitis (citrato de zinc) no afecte la estabilidad y biodisponibilidad en la cavidad oral del agente flúor, y
- Que se dé una disminución de la astringencia debida a la inclusión de copolímero de anhídrido maleico y éter de polivinil metilo por la formación de complejos con el zinc y el compuesto polifosfato.

De esta manera, no basta solo con argumentar que el versado en la materia "decidiría" "incluir sin razón algún citrato de zinc en la formulación de D1 para llegar al objeto de la presente invención, pues se requiere de un análisis a profundidad de las propiedades fisicoquímicas y el objetivo de cada uno de los ingredientes dentro de la formulación, que permita, con una alta expectativa de éxito, concluir que la combinación de agentes es viable y genera los efectos técnicos perseguidos.

Lo anterior es de alta relevancia, pues de acuerdo con el Instructivo de patentabilidad el examinador debe presentar los documentos relevantes que anulan el nivel inventivo de la invención en estudio y el examen de **cómo las divulgaciones previas inducen a la persona del oficio normalmente versada en la materia a realizar la invención sin que se hubiese requerido de su parte investigación alguna**, al tener en cuenta que el normalmente versado en la materia no cuenta con capacidad inventiva.

Lo anterior en definitiva **no** sucede en este caso, pues como se ha expuesto a lo largo del presente memorial, D1 y D2 ignoran por completo tanto la viabilidad de la combinación de los ingredientes esenciales para la presente invención, como los efectos benéficos derivados de dicha combinación.

Por tanto, consideramos que la única vía para llegar a las enseñanzas de la presente invención es mediante la aplicación de un análisis en retrospectiva, en donde, a partir del conocimiento de las características esenciales de la invención se buscan referencias del arte previo que incluyan de manera individual tales características, pero sin considerar que los documentos citados no contemplan ninguna sugerencia para la inclusión de ingredientes adicionales.

Es así como las enseñanzas brindadas por las referencias citadas por su Despacho, y los argumentos del examinador, no explican de ninguna forma la motivación que tendría el normalmente versado en la materia para inclinarse por la inclusión de la combinación de ingredientes de la composición de la presente invención, y por tanto queda demostrado el nivel inventivo de la presente invención a la luz de las enseñanzas de D1 y D2.

En vista de lo anteriormente expuesto, respetuosamente solicitamos el retiro de las objeciones de la presente solicitud y la concesión del privilegio solicitado, ya que en opinión del solicitante cumple con todos los requisitos establecidos en la decisión 486.

Adicionalmente nos permitimos informar al señor Examinador que procederemos a la presentación de una solicitud divisional, en la cual se presenta un pliego reivindicatorio compuesto por 9 reivindicaciones, para que sea objeto de estudio de su Oficina.

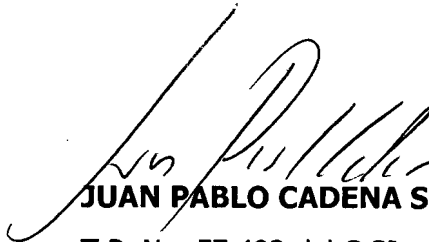
PETICIÓN

Por las razones anteriormente expuestas, solicito a ese despacho **REVOCAR** la decisión tomada mediante la Resolución No. 7912 del 28 de Febrero de 2013 y tendiente a obtener la concesión del Privilegio de Patente de conformidad con los artículos 14 y 48 de la Decisión 486 de la comunidad Andina.

NOTIFICACIONES

Recibiré notificaciones en la Secretaría General de la Superintendencia de Industria y Comercio, o en su defecto, en mi oficina de Abogado, situada en la Calle 70ª No. 4-41 de esta ciudad de Bogotá.

Del Señor Director


JUAN PABLO CADENA SARMIENTO
T.P. No. 57.492 del C.SJ.
C.C. 80.410.337 de Usaquén
Calle 70 A No. 4 - 41

REIVINDICACIONES

1. Una composición oral anti-placa y desensibilizadora que comprende:
 - Un agente de citrato de zinc;
 - Un agente de nitrato de potasio;
 - Un agente fluoruro seleccionado del grupo que consiste de fluoruro de sodio, fluoruro de potasio, monofluorofosfato de sodio, fluorosilicato de sodio, fluoruro de amonio, fluoruro de amina y fluoruro de estaño;
 - Un copolímero de anhídrido maleico y éter de polivinil metilo; y
 - Un polifosfato.
2. La composición de acuerdo con la reivindicación 1, en donde el agente de citrato de zinc comprende un compuesto que tiene la fórmula nominal general de $\text{ZN}_3(\text{C}_6\text{H}_5\text{O}_7)_2$.
3. La composición de acuerdo con cualquiera de las reivindicaciones 1 a 2, que además comprende un compuesto seleccionado de tartrato de potasio, cloruro de potasio, sulfato de potasio, citrato de potasio, nitrato de sodio, citrato de sodio y mezclas de los mismos.
4. La composición de acuerdo con cualquiera de las reivindicaciones 1 a 3, en donde la relación del agente de citrato de zinc al agente de nitrato de potasio es de 0.5:1 a 1:0.5.
5. La composición de acuerdo con cualquiera de las reivindicaciones 1 a 3, en donde el agente de citrato de zinc está presente en una cantidad de 0.001% a 5% en peso de la composición oral y el agente de nitrato de potasio está presente en una cantidad de 0.001% a 10% en peso de la composición oral.
6. La composición de acuerdo con cualquiera de las reivindicaciones 1 a 5, que además comprende un éter de difenilo halogenado no iónico.
7. La composición de acuerdo con cualquiera de las reivindicaciones 1 a 6, en donde la composición oral está en la forma de un enjuague bucal, un dentífrico, un confite, un medicamento o una película.

8. La composición oral de acuerdo con la reivindicación 2, en donde:

- la composición además comprende un compuesto seleccionado de tartrato de potasio, cloruro de potasio, sulfato de potasio, citrato de potasio, nitrato de sodio, citrato de sodio y mezclas de los mismos;
- la relación del agente de citrato de zinc al agente de nitrato de potasio es de 0.5:1 a 1:0.5;
- el agente de citrato de zinc está presente en una cantidad de 0.001% a 5% en peso de la composición oral y el agente de nitrato de potasio está presente en una cantidad de 0.001% a 10% en peso de la composición oral; y
- la composición además comprende un éter de difenilo halogenado no iónico.

9. La composición de acuerdo con la reivindicación 8, en donde la composición oral está en la forma de un enjuague bucal, un dentífrico, un confite, un medicamento o una película.

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**The Comparative Efficacy of a Dentifrice
Containing 2.0% Zinc Citrate, 5.0%
Potassium Nitrate, and 1500 ppm Fluoride as
Sodium Monofluorophosphate and a
Commercially-Available Dentifrice containing
1500 ppm Fluoride as Sodium
Monofluorophosphate in Controlling
Established Plaque and Gingivitis**

A Six-Month Study on Adults in Florida

**Suru Mankodi, DDS, MSD
Salim Nathoo, DDS, PhD
Dental Products Testing
West Palm Beach, Florida**

**Howard M. Proskin, PhD
H.M. Proskin & Associates, Inc.
Rochester, New York**

DATES OF STUDY: March – September, 2011

DATE OF REPORT: December, 2011

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ABSTRACT

The objective of this double-blind, parallel-group clinical study conducted at Dental Products Testing in West Palm Beach, Florida, was to evaluate the clinical efficacy of a dentifrice containing 2.0% zinc citrate, 5.0% potassium nitrate, and 1500 ppm fluoride as sodium monofluorophosphate (SMFP), as compared to a commercially-available dentifrice containing, 1500 ppm fluoride as SMFP in controlling established dental plaque and gingivitis in adults.

Qualifying adult male and female subjects from the West Palm Beach, Florida area were randomly assigned into one of two treatment groups: (1) a dentifrice containing 2.0% zinc citrate, 5.0% potassium nitrate, and 1500 ppm fluoride as SMFP (Test Dentifrice); and (2) a commercially-available dentifrice containing 1500 ppm fluoride as SMFP (Control Dentifrice). All subjects received an oral soft and hard tissue examination, and were dispensed their assigned dentifrice product along with a soft-bristled adult toothbrush for home use. Subjects were instructed to brush their teeth for one minute, twice daily (morning and evening), using only the dentifrice provided. Both examinations for plaque and gingivitis, and assessments of oral soft and hard tissue were repeated after three months and six months of product use.

The statistical analyses were performed on both the intent-to-treat (ITT) and per protocol (PP) populations. The ITT population consisted of all 103 randomized subjects who were dispensed study treatment. The PP population consisted of 93 subjects within the ITT population who had no serious protocol violations, completed all study visits, and for whom data was available for at least one of the clinical indices at all study visits.

ITT Population

After six months of product use, subjects assigned to the Test Dentifrice group exhibited statistically significant reductions ($p < 0.05$) from baseline with respect to plaque and gingival index scores. Subjects assigned to the Control Dentifrice group did not exhibit statistically significant reductions ($p > 0.05$) from baseline with respect to either plaque or gingival index scores.

The Test Dentifrice group exhibited statistically significant reductions in both plaque (20.6%) and gingival (18.9%) index scores after six months of product use.

PP Population

After six months of product use, subjects assigned to the Test Dentifrice group exhibited statistically significant reductions ($p < 0.05$) from baseline with respect to plaque and gingival index scores. Subjects assigned to the Control Dentifrice group did not exhibit statistically significant reductions ($P > 0.05$) from baseline Control with respect to either plaque or gingival index scores.

Relative to the Control Dentifrice group, the Test Dentifrice group exhibited statistically significant reductions ($p < 0.05$) in both plaque (24.2%) and gingival (20.8%) index scores after six months of product use, both of which were statistically significant.

Among subjects who completed the six-month study, the results of this double-blind clinical study support the conclusion that a dentifrice containing 2.0% zinc citrate, 5.0% potassium nitrate, and 1500 ppm fluoride as SMFP provides statistically significant reductions in plaque and gingivitis relative to a commercially-available dentifrice containing fluoride alone as a control, when used over a period of six months

INTRODUCTION

The objective of this clinical study was to evaluate the clinical efficacy of a dentifrice containing 2.0% zinc citrate, 5.0% potassium nitrate, and 1500 ppm fluoride as sodium monofluorophosphate (SMFP) in controlling established dental plaque and gingivitis as compared to a commercially-available control dentifrice containing 1500 ppm fluoride, as SMFP, alone..

MATERIALS AND METHODS

This clinical study, conducted at Dental Products Testing in West Palm Beach, Florida, employed a double-blind, randomized, two-treatment, parallel-group design. Male and female subjects were enrolled into the study based upon the following criteria:

- (i) Subjects had to be between the ages of 18 and 70, in generally good health, and possess a minimum of 20 uncrowned permanent natural teeth (excluding third molars).
- (ii) Subjects needed to be available for the six-month duration of the study, and to sign an informed consent form.
- (iii) Subjects were required to present a mean Löe-Silness Gingival Index score of at least 1.0, and a mean plaque index score of 1.5 or greater as determined by the use of the Turesky modification of the Quigley-Hein Plaque Index at the baseline examination.
- (iv) Subjects were excluded from the study if they had orthodontic bands, presence of partial removable dentures, tumor(s) of the soft or hard tissues of the oral cavity, advanced periodontal disease (purulent exudates, tooth mobility and/or extensive loss of periodontal attachment or alveolar bone), five or more carious lesions requiring immediate restorative treatment.
- (v) Subjects with a history of allergy to personal care/consumer products or their ingredients, or with existing medical conditions which precluded them from not eating and drinking for periods up to four hours, or who were taking any prescription medication that might interfere with the study outcome were excluded from the study. Additionally, pregnant or lactating women were excluded from participation.
- (vi) Subjects were excluded if they had used antibiotics or participated in any other clinical study or test panel within one month prior to entry into the study, or if they had received a dental prophylaxis within two weeks prior to entry into the study.

Prospective study subjects reported to the clinical facility having refrained from all oral hygiene procedures for twelve hours, and having refrained from eating, drinking or smoking for four hours prior to their examination. All prospective subjects who met the inclusion/exclusion criteria, signed an informed consent form, and completed a medical history questionnaire received a baseline plaque and gingivitis examination, along with an oral soft and hard tissue assessment. All subjects who signed an informed consent form were provided with a copy of their signed form for their records.

Qualifying subjects were stratified into two balanced groups based on their baseline plaque and gingival index scores, and were randomly assigned within strata to one of two study treatments. For the purpose of this report, the treatments are identified as follows:

**Test
Dentifrice**

A dentifrice containing 2.0% zinc citrate, 5.0% potassium nitrate, and 1500 ppm fluoride as SMFP [PDM# 1*19777] (Colgate-Palmolive Co., New York, NY).

**Control
Dentifrice**

A commercially available dentifrice containing 1500 ppm fluoride as MFP [PIM# 427679] (Colgate Cavity Protection Toothpaste, Colgate-Palmolive Co., New York, NY)

Following study treatment assignment, subjects were provided with their assigned dentifrice and an adult, soft-bristled toothbrush for home use. Both of the dentifrice products were supplied in their original packaging and overwrapped with a white label to mask the product's identity. Subjects were instructed to brush their teeth for one minute, twice daily (morning and evening) using only the dentifrice and toothbrush provided, and to refrain from any other oral hygiene procedures throughout the duration of the study. There were no restrictions regarding diet or smoking habits during the course of the study, except as indicated above.

After three months, and again after six months of product use, subjects returned to the clinical facility for plaque and gingivitis examinations, and oral soft and hard tissue assessments. Examinations were performed by the same dental examiner, using the same procedures as employed at baseline. At each examination, subjects were interviewed with respect to any changes in medical history, the presence of adverse events, and the use of concomitant medications.

CLINICAL SCORING PROCEDURES

Plaque Assessment

Supragingival plaque on the facial and lingual surfaces of each tooth was scored according to the Turesky modification of the Quigley-Hein Plaque Index^{1,2}. Each tooth was divided into six surfaces, three facially and three lingually, as follows: 1) mesio-facial; 2) mid-facial; 3) disto-facial; 4) mesio-lingual; 5) mid-lingual; and 6) disto-lingual. Third molars and those teeth with cervical restorations or prosthetic crowns were excluded from the scoring procedure. Plaque was disclosed and scored on each tooth surface according to the following criteria:

- 0 = No plaque.
- 1 = Separate flecks of plaque at the cervical margin of the tooth.
- 2 = A thin, continuous band of plaque (up to 1 mm) at the cervical margin of the tooth.
- 3 = A band of plaque wider than 1 mm, but covering less than 1/3 of the side of the crown of the tooth.
- 4 = Plaque covering at least 1/3, but less than 2/3 of the side of the crown of the tooth.
- 5 = Plaque covering 2/3 or more of the side of the crown of the tooth.

Whole-mouth mean scores were obtained by averaging the values obtained over all scoreable surfaces in the mouth.

Figure 1 illustrates the form which was used to record the Quigley-Hein Plaque Index scores in this study.

Gingivitis Assessment

Gingivitis was scored according to the Löe-Silness Gingival Index^{3,4}. Each tooth was divided into six surfaces, three facially and three lingually, as follows: 1) mesio-facial; 2) mid-facial; 3) disto-facial; 4) mesio-lingual; 5) mid-lingual; and 6) disto-lingual. Third molars and those teeth with cervical restorations or prosthetic crowns were excluded from the scoring procedure. The gingiva adjacent to each tooth surface was scored as follows:

- 0 = Absence of inflammation.
- 1 = Mild inflammation: slight change in color and little change in texture.
- 2 = Moderate inflammation: moderate glazing, redness, edema, hypertrophy. Tendency to bleed upon probing.
- 3 = Severe inflammation: marked redness and hypertrophy. Tendency for spontaneous bleeding.

Whole-mouth mean scores were obtained by averaging the values obtained over all scoreable surfaces in the mouth.

Figure 2 illustrates the form which was used to record the Löe-Silness Gingival Index scores in this study.

Oral Soft and Hard Tissue Assessment

The dental examiner visually examined the oral cavity and peri-oral area using a dental light and dental mirror. This examination evaluation included an assessment of the soft and hard palate, gingival mucosa, buccal mucosa, mucogingival fold areas, tongue, sublingual and submandibular areas, salivary glands, and the tonsillar and pharyngeal areas of the mouth.

Adverse Events

Adverse events were obtained from an interview with the subject and a dental examination by the investigator.

STATISTICAL METHODS

Statistical analyses were performed separately for the plaque and gingival indices on both the intent-to-treat (ITT) and per protocol (PP) populations.

The ITT population consisted of all randomized subjects who were dispensed study treatment. For the analyses performed on the ITT population, any missing values were imputed by carrying forward the values from the last-observed previous examination (LOCF).

The PP population consisted of those subjects in the ITT population who had no serious protocol violations, completed all study visits, and for whom data was available for at least one of the clinical indices at all study visits. For the analyses performed on the PP population, missing values were not imputed. If a subject did not have sufficient data for a particular analysis, then that subject was excluded from that analysis.

Comparisons of the treatment groups with respect to baseline plaque and gingival index scores, as well as for age, were performed using analyses of variance (ANOVA's). Comparisons between the treatment groups with respect to gender and race were performed using chi-squared tests. Within-treatment comparisons of the plaque and gingival index scores obtained at the follow-up examinations versus baseline were performed using paired t-tests. Comparisons of the treatment groups with respect to baseline-adjusted plaque and gingival index scores at the follow-up examinations were performed using analyses of covariance (ANCOVA's). All statistical tests of hypotheses were two sided, and employed a level of significance of $\alpha=0.05$.

RESULTS

Subject Disposition

A summary of subject disposition is provided in Table 1. Of the 110 subjects who were screened for inclusion in the study, 103 subjects were randomized, dispensed study treatment, and included in the ITT population. The ITT population consisted of 52 subjects randomized to the Test Dentifrice group, and 51 subjects randomized to the Control Dentifrice group. A total of 10 subjects (6 in the Test Dentifrice group, and 4 in the Control Dentifrice group) were discontinued from the study.

There were 93 subjects who completed all study visits, had no major protocol violations, and were included in the PP population. The PP population consisted of 46 subjects randomized to the Test Dentifrice group, and 47 subjects randomized to the Control Dentifrice group.

Demographics

ITT Population

A summary of the gender, age, and race of subjects in the ITT population is presented in Table 2.

For subjects in the Test Dentifrice group, the mean age of the subjects was 43.7 with a range of 19 to 66 years. The majority of subjects were female, and the predominant race was Caucasian, followed by African American.

For subjects in the Control Dentifrice group, the mean age of the subjects was 38.3 with a range of 18 to 61 years. The majority of subjects were female, and the predominant race was Caucasian, followed by Hispanic.

A statistically significant difference ($p < 0.05$) was indicated between the two treatment groups at baseline with respect to age and race.

PP Population

A summary of the gender, age, and race of subjects in the PP population is presented in Table 3.

For subjects in the Test Dentifrice group, the mean age of the subjects was 44.0 with a range of 21 to 66 years. The majority of subjects were female, and the predominant race was Caucasian, followed by African American.

For subjects in the Control Dentifrice group, the mean age of the subjects was 38.0 with

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a range of 18 to 61 years. The majority of subjects were female, and the predominant race was Caucasian, followed by Hispanic.

A statistically significant difference was indicated between the two treatment groups at baseline with respect to age and race.

Baseline Data

ITT Population

Table 4 presents a summary of the plaque and gingival index scores measured at the baseline examination for those subjects in the ITT population.

The mean baseline plaque index scores were 2.26 for the Test Dentifrice group and 2.20 for the Control Dentifrice group. No statistically significant difference was indicated between the treatment groups with respect to the mean baseline plaque index scores.

The mean baseline gingival index scores were 1.07 for the Test Dentifrice group and 1.07 for the Control Dentifrice group. No statistically significant difference was indicated between the treatment groups with respect to the mean baseline gingival index scores.

PP Population

Table 5 presents a summary of the plaque index and gingival index scores measured at the baseline examination for those subjects in the PP population.

The mean baseline plaque index scores were 2.25 for the Test Dentifrice group and 2.18 for the Control Dentifrice group. No statistically significant difference was indicated between the treatment groups with respect to the mean baseline plaque index scores.

The mean baseline gingival index scores were 1.06 for the Test Dentifrice group and 1.07 for the Control Dentifrice group. No statistically significant difference was indicated between the treatment groups with respect to the mean baseline gingival index scores.

Three-Month Data

Plaque Index

ITT Population

Table 6 presents a summary of the plaque index scores measured at the three-month examination for those subjects in the ITT population.

Comparisons versus baseline: The mean three-month plaque index scores were 1.95 for the

Test Dentifrice group and 2.15 for the Control Dentifrice group. The mean percent reduction from baseline was 13.7% for the Test Dentifrice group, which was statistically significant ($p < 0.05$). For the Control Dentifrice group, the mean percent reduction from baseline was 2.3%, which was not statistically significant ($p > 0.05$).

Comparison between treatment groups: Relative to the Control Dentifrice group, the Test Dentifrice group exhibited a statistically significant 9.3% reduction ($p < 0.05$) in plaque index scores after three months of product use.

PP Population

Table 7 presents a summary of the plaque index scores measured at the three-month examination for those subjects in the PP population.

Comparisons versus baseline: The mean three-month plaque index scores were 1.92 for the Test Dentifrice group and 2.16 for the Control Dentifrice group. The mean percent reduction from baseline was 14.7% for the Test Dentifrice group, which was statistically significant ($p < 0.05$). For the Control Dentifrice group, the mean percent reduction from baseline was 0.9%, which was not statistically significant ($p > 0.05$).

Comparison between treatment groups: Relative to the Control Dentifrice group, the Test Dentifrice group exhibited a statistically significant 11.1% reduction in plaque index scores after three months of product use.

Gingival index

ITT Population

Table 8 presents a summary of the gingival index scores measured at the three-month examination for those subjects in the ITT population.

Comparisons versus baseline: The mean three-month gingival index scores were 0.94 for the Test Dentifrice group and 1.06 for the Control Dentifrice group. The mean percent reduction from baseline was 12.1% for the Test Dentifrice group, which was statistically significant ($p < 0.05$). For the Control Dentifrice group, the mean percent reduction from baseline was 0.9%, which was not statistically significant ($p > 0.05$).

Comparison between treatment groups: Relative to the Control Dentifrice group, the Test Dentifrice group exhibited a statistically significant 11.3% reduction ($p < 0.05$) in gingival index scores after three months of product use.

PP Population

Table 9 presents a summary of the gingival index scores measured at the three-month

examination for those subjects in the PP population.

Comparisons versus baseline: The mean three-month gingival index scores were 0.94 for the Test Dentifrice group and 1.06 for the Control Dentifrice group. The mean percent reduction from baseline was 11.3% for the Test Dentifrice group, which was statistically significant ($p<0.05$). For the Control Dentifrice group, the mean percent reduction from baseline was 0.9%, which was not statistically significant ($p>0.05$).

Comparison between treatment groups: Relative to the Control Dentifrice group, the Test Dentifrice group exhibited a statistically significant 11.3% reduction ($p<0.05$) in gingival index scores after three months of product use.

Six-Month Data

Plaque Index

ITT Population

Table 10 presents a summary of the plaque index scores measured at the six-month examination for those subjects in the ITT population.

Comparisons versus baseline: The mean six-month plaque index scores were 1.70 for the Test Dentifrice group and 2.14 for the Control Dentifrice group. The mean percent reduction from baseline was 24.8% for the Test Dentifrice group, which was statistically significant ($p<0.05$). For the Control Dentifrice group, the mean percent reduction from baseline was 2.7%, which was not statistically significant ($p>0.05$).

Comparison between treatment groups: Relative to the Control Dentifrice group, the Test Dentifrice group exhibited a statistically significant 20.6% reduction ($p<0.05$) in plaque index scores after six months of product use.

PP Population

Table 11 presents a summary of the plaque index scores measured at the six-month examination for those subjects in the PP population.

Comparisons versus baseline: The mean six-month plaque index scores were 1.63 for the Test Dentifrice group and 2.15 for the Control Dentifrice group. The mean percent reduction from baseline was 27.6% for the Test Dentifrice group, which was statistically significant ($p<0.05$). For the Control Dentifrice group, the mean percent reduction from baseline was 1.4%, which was not statistically significant ($p>0.05$).

Comparison between treatment groups: Relative to the Control Dentifrice group, the Test Dentifrice group exhibited a statistically significant 24.2% reduction ($p<0.05$) in plaque index

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scores after six months of product use.

Gingival index

ITT Population

Table 12 presents a summary of the gingival index scores measured at the six-month examination for those subjects in the ITT population.

Comparisons versus baseline: The mean six-month gingival index scores were 0.86 for the Test Dentifrice group and 1.06 for the Control Dentifrice group. The mean percent reduction from baseline was 19.6% for the Test Dentifrice group, which was statistically significant ($p < 0.05$). For the Control Dentifrice group, the mean percent reduction from baseline was 0.9%, which was not statistically significant ($p > 0.05$).

Comparison between treatment groups: Relative to the Control Dentifrice group, the Test Dentifrice group exhibited a statistically significant 18.9% reduction ($p < 0.05$) in gingival index scores after six months of product use.

PP Population

Table 13 presents a summary of the gingival index scores measured at the six-month examination for those subjects in the PP population.

Comparisons versus baseline: The mean six-month gingival index scores were 0.84 for the Test Dentifrice group and 1.06 for the Control Dentifrice group. The mean percent reduction from baseline was 20.8% for the Test Dentifrice group, which was statistically significant ($p < 0.05$). For the Control Dentifrice group, the mean percent reduction from baseline was 0.9%, which was not statistically significant ($p > 0.05$).

Comparison between treatment groups: Relative to the Control Dentifrice group, the Test Dentifrice group exhibited a statistically significant 20.8% reduction ($p < 0.05$) in gingival index scores after six months of product use.

Oral Soft and Hard Tissue Assessments

There were no abnormal oral hard or soft tissue findings reported during the study.

Adverse Events

Table 14 provides a listing of adverse events reported during the study. Four adverse events were reported involving only three subjects.

One adverse event was reported for a subject in the Test Dentifrice group. The subject experienced tooth sensitivity for fourteen days, which was considered possibly related to the

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study treatment. The subject was permitted to continue in the study by the investigator, and completed the remaining five months of the study without any further events being reported.

The remaining three adverse events were reported for two subjects in the Control Dentifrice group. One subject reported a fractured right ankle, which was not related to the study treatment, and the subject completed the study. The second subject reported a sinus infection and ganglioma cystectomy of the left hand; both events were deemed not related to study treatment. However, this second subject was discontinued from the study due to antibiotic use.

OVERALL FINDINGS AND CONCLUSION

This double-blind clinical study provided a comparison of two dentifrices with respect to the control of established plaque and gingivitis.

Qualifying adult male and female subjects from the West Palm Beach, Florida area were randomly assigned into one of two treatment groups: (1) a dentifrice containing 2.0% zinc citrate, 5.0% potassium nitrate, and 1500 ppm fluoride as SMFP (Test Dentifrice); and (2) a commercially-available dentifrice containing 1500 ppm fluoride as MFP (Control Dentifrice). All subjects received an oral soft and hard tissue examination, and were dispensed their assigned dentifrice product along with a soft-bristled adult toothbrush for home use. Subjects were instructed to brush their teeth for one minute, twice daily (morning and evening), using only the dentifrice provided. Both examinations for plaque and gingivitis, and oral soft and assessments of hard tissue were repeated after three months, and six months of product use.

The statistical analyses were performed on both the intent-to-treat (ITT) and per protocol (PP) populations. The ITT population consisted of all 103 randomized subjects who were dispensed study treatment. The PP population consisted of 93 subjects within the ITT population who had no serious protocol violations, completed all study visits, and for whom data was available for at least one of the clinical indices at all study visits.

ITT Population

After both three months and six months of product use, subjects assigned to the Test Dentifrice group exhibited statistically significant reductions from baseline with respect to plaque and gingival index scores. Subjects assigned to the Control Dentifrice group did not exhibit statistically significant reductions from baseline Control with respect to either plaque or gingival index scores.

Relative to the Control Dentifrice group, the Test Dentifrice group exhibited a 9.3% reduction in plaque index scores after three months of product use, and a 20.6% reduction in plaque index scores after six months of product use, both of which were statistically significant.

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Relative to the Control Dentifrice group, the Test Dentifrice group exhibited an 11.3% reduction in gingival index scores after three months of product use, and an 18.9% reduction in gingival index scores after six months, both of which were statistically significant.

PP Population

After both three months and six months of product use, subjects assigned to the Test Dentifrice group exhibited statistically significant reductions from baseline with respect to plaque and gingival index scores. Subjects assigned to the Control Dentifrice group did not exhibit statistically significant reductions from baseline Control with respect to either plaque or gingival index scores.

Relative to the Control Dentifrice group, the Test Dentifrice group exhibited an 11.1% reduction in plaque index scores after three months of product use, and a 24.2% reduction in plaque index scores after six months of product use, both of which were statistically significant.

Relative to the Control Dentifrice group, the Test Dentifrice group exhibited an 11.3% reduction in gingival index scores after three months of product use, and a 20.8% reduction in gingival index scores after six months of product use, both of which were statistically significant.

Among subjects who completed the six-month study, the results of this double-blind clinical study support the conclusion that a dentifrice containing 2.0% zinc citrate, 5.0% potassium nitrate, and 1500 ppm fluoride as SMFP provides a statistically significant reduction in plaque and gingivitis compared to a commercially-available dentifrice with 1500 ppm fluoride alone when used over a period of six months. .

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STUDY SPONSOR

This clinical study was sponsored by the Colgate-Palmolive Company.

Study Director: William DeVizio, DMD

Study Monitor: Pat Chaknis, BS

Identification of Tested Products:

**Test
Dentifrice**

A dentifrice containing 2.0% zinc citrate, 5.0% potassium nitrate, and 1500 ppm fluoride as SMFP [PDM# 1*19777] (Colgate-Palmolive Co., New York, NY).

**Control
Dentifrice**

A commercially-available dentifrice containing 1500 ppm fluoride as MFP [PIM# 427679] (Colgate Cavity Protection Toothpaste, Colgate-Palmolive Co., New York, NY).

Table 1
Disposition of Subjects

	Test Dentifrice ¹	Control Dentifrice ²	Total
Screened	110		110
Randomized (ITT Population)	52	51	103
Completed (PP Population)	46	47	93
Discontinued	6	4	10

¹ A dentifrice containing 2.0% zinc citrate, 5.0% potassium nitrate, and 1500 ppm fluoride as SMFP (Colgate-Palmolive Co., New York, NY).

² A commercially-available dentifrice containing 1500 ppm fluoride as SMFP (Colgate-Palmolive Co., New York, NY).

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Table 2
Summary of Gender, Age, and Race
ITT Population

Treatment	Number of Subjects			Age		Race				
	Male	Female	Total	Mean ³	Range	Asian	Black	Caucasian	Hispanic	Other
Test Dentifrice ¹	9	43	52	43.7	19 - 66	5	11	32	3	1
Control Dentifrice ²	10	41	51	38.3	18 - 61	1	12	24	13	1

¹ A dentifrice containing 2.0% zinc citrate, 5.0% potassium nitrate, and 1500 ppm fluoride as SMFP (Colgate-Palmolive Co., New York, NY).

² A commercially-available dentifrice containing 1500 ppm fluoride as SMFP (Colgate-Palmolive Co., New York, NY).

³ A statistically significant difference (p<0.05) was indicated between the two treatment groups at baseline with respect to age and race

Table 3
Summary of Gender, Age, and Race
PP Population

Treatment	Number of Subjects			Age		Race				
	Male	Female	Total	Mean ³	Range	Asian	Black	Caucasian	Hispanic	Other
Test Dentifrice ¹	9	37	46	44.0	21 - 66	5	10	29	2	0
Control Dentifrice ²	8	39	47	38.0	18 - 61	1	12	20	13	1

- ¹ A dentifrice containing 2.0% zinc citrate, 5.0% potassium nitrate, and 1500 ppm fluoride as SMFP (Colgate-Palmolive Co., New York, NY).
- ² A commercially-available dentifrice containing 1500 ppm fluoride as SMFP Colgate-Palmolive Co., New York, NY).
- ³ A statistically significant difference ($p<0.05$) was indicated between the two treatment groups at baseline with respect to age and race.

Table 4
Summary of the Baseline Plaque and Gingival index Scores
ITT Population

Parameter	Treatment	n	Baseline Summary (Mean ± S.D.) ³	
Plaque Index	Test Dentifrice ¹	52	2.26	± 0.41
	Control Dentifrice ²	51	2.20	± 0.35
Gingival Index	Test Dentifrice ¹	52	1.07	± 0.07
	Control Dentifrice ²	51	1.07	± 0.06

¹ A dentifrice containing 2.0% zinc citrate, 5.0% potassium nitrate, and 1500 ppm fluoride as SMFP (Colgate-Palmolive Co., New York, NY).

² A commercially-available dentifrice containing 1500 ppm fluoride as SMFP (Colgate-Palmolive Co., New York, NY).

³ No statistically significant difference (p>0.05) was indicated between the two treatment groups at baseline with respect to either plaque or gingival index scores.

Table 5
Summary of the Baseline Plaque and Gingival index Scores
PP Population

Parameter	Treatment	n	Baseline Summary (Mean ± S.D.) ³
Plaque Index	Test Dentifrice ¹	46	2.25 ± 0.39
	Control Dentifrice ²	47	2.18 ± 0.35
Gingival index	Test Dentifrice ¹	46	1.06 ± 0.07
	Control Dentifrice ²	47	1.07 ± 0.06

¹ A dentifrice containing 2.0% zinc citrate, 5.0% potassium nitrate, and 1500 ppm fluoride as SMFP (Colgate-Palmolive Co., New York, NY).
² A commercially-available dentifrice containing 1500 ppm fluoride as SMFP (Colgate-Palmolive Co., New York, NY).
³ No statistically significant difference (p<0.05) was indicated between the two treatment groups at baseline with respect to either plaque or gingival index scores.

Table 6
Summary of the Three-Month Plaque Index Scores
ITT Population

Treatment	n	Three-Month Summary (Mean ± S.D.)	Within-Treatment Analysis		Between-Treatment Comparison	
			Percent Reduction ³	Sig. ⁴	Percent Reduction ⁵	Sig. ⁶
Test Dentifrice ¹	52	1.95 ± 0.44	13.7%	p<0.05	9.3%	p<0.05
Control Dentifrice ²	51	2.15 ± 0.39	2.3%	NS		

¹ A dentifrice containing 2.0% zinc citrate, 5.0% potassium nitrate, and 1500 ppm fluoride as SMFP (Colgate-Palmolive Co., New York, NY).

² A commercially-available dentifrice containing 1500 ppm fluoride as SMFP (Colgate-Palmolive Co., New York, NY).

³ Percent reduction exhibited by the three-month mean relative to the baseline mean. A positive value indicates a lower plaque index score at the three-month examination.

⁴ Significance of paired t-test comparing the baseline and three-month examinations. NS = p>0.05.

⁵ Between-treatment reduction expressed as a percentage of the three-month mean for Control Dentifrice. A positive value indicates a lower plaque index score for Test Dentifrice than for Control Dentifrice.

⁶ Significance of post-ANCOVA comparison of baseline-adjusted means.

Table 7
Summary of the Three-Month Plaque Index Scores
PP Population

Treatment	n	Three-Month Summary (Mean ± S.D.)	Within-Treatment Analysis		Between-Treatment Comparison	
			Percent Reduction ³	Sig. ⁴	Percent Reduction ⁵	Sig. ⁶
Test Dentifrice ¹	46	1.92 ± 0.45	14.7%	p<0.05	11.1%	p<0.05
Control Dentifrice ²	47	2.16 ± 0.39	0.9%	NS		

¹ A dentifrice containing 2.0% zinc citrate, 5.0% potassium nitrate, and 1500 ppm fluoride as SMFP (Colgate-Palmolive Co., New York, NY).

² A commercially-available dentifrice containing 1500 ppm fluoride as SMFP (Colgate-Palmolive Co., New York, NY).

³ Percent reduction exhibited by the three-month mean relative to the baseline mean. A positive value indicates a lower plaque index score at the three-month examination.

⁴ Significance of paired t-test comparing the baseline and three-month examinations. NS = p>0.05.

⁵ Between-treatment reduction expressed as a percentage of the three-month mean for Control Dentifrice. A positive value indicates a lower plaque index score for Test Dentifrice than for Control Dentifrice.

⁶ Significance of post-ANCOVA comparison of baseline-adjusted means.

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Table 8

Summary of the Three-Month Gingival Index Scores
ITT Population

Treatment	n	Three-Month Summary (Mean ± S.D.)	Within-Treatment Analysis		Between-Treatment Comparison	
			Percent Reduction ³	Sig. ⁴	Percent Reduction ⁵	Sig. ⁶
Test Dentifrice ¹	52	0.94 ± 0.10	12.1%	p<0.05	11.3%	p<0.05
Control Dentifrice ²	51	1.06 ± 0.09	0.9%	NS		

¹ A dentifrice containing 2.0% zinc citrate, 5.0% potassium nitrate, and 1500 ppm fluoride as SMFP (Colgate-Palmolive Co., New York, NY).

² A commercially-available dentifrice containing 1500 ppm fluoride as SMFP (Colgate-Palmolive Co., New York, NY).

³ Percent reduction exhibited by the three-month mean relative to the baseline mean. A positive value indicates a lower gingival index score at the three-month examination.

⁴ Significance of paired t-test comparing the baseline and three-month examinations. NS = p>0.05.

⁵ Between-treatment reduction expressed as a percentage of the three-month mean for Control Dentifrice. A positive value indicates a lower gingival index score for Test Dentifrice than for Control Dentifrice.

⁶ Significance of post-ANCOVA comparison of baseline-adjusted means.

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Table 9

Summary of the Three-Month Gingival index Scores
PP Population

Treatment	n	Three-Month Summary (Mean ± S.D.)	Within-Treatment Analysis		Between-Treatment Comparison	
			Percent Reduction ³	Sig. ⁴	Percent Reduction ⁵	Sig. ⁶
Test Dentifrice ¹	46	0.94 ± 0.10	11.3%	p<0.05	11.3%	p<0.05
Control Dentifrice ²	47	1.06 ± 0.09	0.9%	NS		

- ¹ A dentifrice containing 2.0% zinc citrate, 5.0% potassium nitrate, and 1500 ppm fluoride as SMFP (Colgate-Palmolive Co., New York, NY).
- ² A commercially-available dentifrice containing 1500 ppm fluoride as SMFP (Colgate-Palmolive Co., New York, NY).
- ³ Percent reduction exhibited by the three-month mean relative to the baseline mean. A positive value indicates a lower gingival index score at the three-month examination.
- ⁴ Significance of paired t-test comparing the baseline and three-month examinations. NS = p>0.05.
- ⁵ Between-treatment reduction expressed as a percentage of the three-month mean for Control Dentifrice. A positive value indicates a lower gingival index score for Test Dentifrice than for Control Dentifrice.
- ⁶ Significance of post-ANCOVA comparison of baseline-adjusted means.

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Table 10
Summary of the Six-Month Plaque Index Scores
ITT Population

Treatment	n	Six-Month Summary (Mean ± S.D.)	Within-Treatment Analysis		Between-Treatment Comparison	
			Percent Reduction ³	Sig. ⁴	Percent Reduction ⁵	Sig. ⁶
Test Dentifrice ¹	52	1.70 ± 0.43	24.8%	p<0.05	20.6%	p<0.05
Control Dentifrice ²	51	2.14 ± 0.42	2.7%	NS		

¹ A dentifrice containing 2.0% zinc citrate, 5.0% potassium nitrate, and 1500 ppm fluoride as SMFP (Colgate-Palmolive Co., New York, NY).

² A commercially-available dentifrice containing 1500 ppm fluoride as SMFP (Colgate-Palmolive Co., New York, NY).

³ Percent reduction exhibited by the six-month mean relative to the baseline mean. A positive value indicates a lower plaque index score at the six-month examination.

⁴ Significance of paired t-test comparing the baseline and six-month examinations. NS = p>0.05.

⁵ Between-treatment reduction expressed as a percentage of the six-month mean for Control Dentifrice. A positive value indicates a lower plaque index score for Test Dentifrice than for Control Dentifrice.

⁶ Significance of post-ANCOVA comparison of baseline-adjusted means.

Table 11
Summary of the Six-Month Plaque Index Scores
PP Population

Treatment	n	Six-Month Summary (Mean ± S.D.)	Within-Treatment Analysis		Between-Treatment Comparison	
			Percent Reduction ³	Sig. ⁴	Percent Reduction ⁵	Sig. ⁶
Test Dentifrice ¹	46	1.63 ± 0.41	27.6%	p<0.05	24.2%	p<0.05
Control Dentifrice ²	47	2.15 ± 0.42	1.4%	NS		

¹ A dentifrice containing 2.0% zinc citrate, 5.0% potassium nitrate, and 1500 ppm fluoride as SMFP (Colgate-Palmolive Co., New York, NY).

² A commercially-available dentifrice containing 1500 ppm fluoride as SMFP (Colgate-Palmolive Co., New York, NY).

³ Percent reduction exhibited by the six-month mean relative to the baseline mean. A positive value indicates a lower plaque index score at the six-month examination.

⁴ Significance of paired t-test comparing the baseline and six-month examinations. NS = p>0.05.

⁵ Between-treatment reduction expressed as a percentage of the six-month mean for Control Dentifrice. A positive value indicates a lower plaque index score for Test Dentifrice than for Control Dentifrice.

⁶ Significance of post-ANCOVA comparison of baseline-adjusted means.

ah

Table 12
Summary of the Six-Month Gingival Index Scores
ITT Population

Treatment	n	Six-Month Summary (Mean ± S.D.)	Within-Treatment Analysis		Between-Treatment Comparison	
			Percent Reduction ³	Sig. ⁴	Percent Reduction ⁵	Sig. ⁶
Test Dentifrice ¹	52	0.86 ± 0.13	19.6%	p<0.05	18.9%	p<0.05
Control Dentifrice ²	51	1.06 ± 0.09	0.9%	NS		

¹ A dentifrice containing 2.0% zinc citrate, 5.0% potassium nitrate, and 1500 ppm SMFP fluoride as (Colgate-Palmolive Co., New York, NY).

² A commercially-available dentifrice containing 1500 ppm fluoride as SMFP (Colgate-Palmolive Co., New York, NY).

³ Percent reduction exhibited by the six-month mean relative to the baseline mean. A positive value indicates a lower gingival index score at the six-month examination.

⁴ Significance of paired t-test comparing the baseline and six-month examinations. NS = p>0.05.

⁵ Between-treatment reduction expressed as a percentage of the six-month mean for Control Dentifrice. A positive value indicates a lower gingival index score for Test Dentifrice than for Control Dentifrice.

⁶ Significance of post-ANCOVA comparison of baseline-adjusted means.

Table 13
Summary of the Six-Month Gingival Index Scores
PP Population

Treatment	n	Six-Month Summary (Mean ± S.D.)	Within-Treatment Analysis		Between-Treatment Comparison	
			Percent Reduction ³	Sig. ⁴	Percent Reduction ⁵	Sig. ⁶
Test Dentifrice ¹	46	0.84 ± 0.12	20.8%	p<0.05	20.8%	p<0.05
Control Dentifrice ²	47	1.06 ± 0.09	0.9%	NS		

¹ A dentifrice containing 2.0% zinc citrate, 5.0% potassium nitrate, and 1500 ppm fluoride as SMFP (Colgate-Palmolive Co., New York, NY).

² A commercially-available dentifrice containing 1500 ppm fluoride as SMFP (Colgate-Palmolive Co., New York, NY).

³ Percent reduction exhibited by the six-month mean relative to the baseline mean. A positive value indicates a lower gingival index score at the six-month examination.

⁴ Significance of paired t-test comparing the baseline and six-month examinations. NS = p>0.05.

⁵ Between-treatment reduction expressed as a percentage of the six-month mean for Control Dentifrice. A positive value indicates a lower gingival index score for Test Dentifrice than for Control Dentifrice.

⁶ Significance of post-ANCOVA comparison of baseline-adjusted means.

Table 14
Listing of Adverse Events

Subject #	Treatment	Adverse Event Description	Date Began	Date Resolved	Relationship to Study Product	Comments
474	Control Dentifrice ²	Fx R Ankle	30/Apr/2011	10/Sep/2011	Not Related	Continued per examiner
478	Test Dentifrice ¹	Teeth Sensitivity	02/Apr/2011	16/Apr/2011	Possibly Related	Continued per examiner
481	Control Dentifrice ²	Sinus Infection	10/Jun/2011	15/Jun/2011	Not Related	Continued per examiner
		Ganglioma Cystectomy L Hand	21/Jul/2011	21/Jul/2011	Not Related	Dropped per Examiner for antibiotic use.

¹ A dentifrice containing 2.0% zinc citrate, 5.0% potassium nitrate, and 1500 ppm fluoride as SMFP (Colgate-Palmolive Co., New York, NY).
² A commercially-available dentifrice containing 1500 ppm fluoride as SMFP (Colgate-Palmolive Co., New York, NY).

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FIGURE LEGENDS

Figure 1

Quigley-Hein Plaque Index examination form.

Figure 2

Löe-Silness Gingival Index examination form.

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Figure 1
Quigley-Hein

Plaque

Index

Scoring

Form

PLAQUE EXAM FORM

Date _____ Subject Name _____ No. _____

Baseline ☐ Mid-study ☐ Final ☐

UPPER TEETH																
Tooth #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Facial Surface Score																
Lingual Surface Score																

LOWER TEETH																
Tooth #	32	31	30	29	28	27	26	25	24	23	22	21	20	19	18	17
Facial Surface Score																
Lingual Surface Score																

If tooth is missing, place **X** in scorebox

(See other side for Modified Quigley-Hein Plaque Scoring Procedure)

Name of Dental Clinic

Signature of Examining Dentist

Property of Colgate-Palmolive

Y6

Figure 1 Cont'd

PLAQUE INDEX CALCULATION

Sum of all scores for all sites

Total number of sites scored

=

=

Plaque Index

The Modified Quigley-Hein criteria for the plaque index are as follows:

- 0 = No plaque.
- 1 = Separate flecks of plaque at the cervical margin of the tooth.
- 2 = A thin continuous band of plaque (up to one mm) at the cervical margin of the tooth.
- 3 = A band of plaque wider than one mm but covering less than one-third of the crown of the tooth.
- 4 = Plaque covering at least one-third but less than two-thirds of the crown of the tooth.
- 5 = Plaque covering two-thirds or more of the crown of the tooth.

Quigley GA, Hein JW: Comparative cleansing efficacy of manual and power brushing. *JADA* 65:26-29, 1962.

Turesky S, Gilmore ND, Glickman I: Reduced plaque formation by the chloromethyl analogue of vitamin C. *J Periodontol* 41:41-43, 1970.

Tooth	32	31
Facial Surface Score		

↔ MESIAL PLAQUE SCORE

↔ MIDDLE PLAQUE SCORE

↔ DISTAL PLAQUE SCORE

Figure 2
Löe-Silness Gingival Index Scoring
Form

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GINGIVITIS EXAM FORM

Date _____ Subject Name _____ No. _____

Baseline ☐ Mid-study ☐ Final ☐

UPPER TEETH																
Tooth #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Facial Surface Score	X															X
Lingual Surface Score	X															X

LOWER TEETH																
Tooth #	32	31	30	29	28	27	26	25	24	23	22	21	20	19	18	17
Facial Surface Score	X															X
Lingual Surface Score	X															X

If tooth is missing, place **X** in scorebox (See other side for Löe-Silness Gingivitis Scoring Procedure)

Name of Dental Clinic

Signature of Examining Dentist

Property of Colgate-Palmolive

Figure 2 Cont'd

GINGIVITIS INDEX CALCULATION

Sum of all scores for all surfaces

=

Gingivitis Index

Total number of surfaces scored

=

Per surface

The Loe-Silness criteria for the gingival index are as follows:

- 0 = Absence of inflammation.
- 1 = Mild inflammation - slight change in color and little change in texture.
- 2 = Moderate inflammation - moderate glazing, redness, edema and hypertrophy.
Tendency to bleed upon probing.
- 3 = Severe inflammation - marked redness and hypertrophy.
Tendency to spontaneous bleeding.

Loe H, Silness J: Periodontal disease in pregnancy. I. Prevalence and severity. *Acta Odont Scand* 21:533-551, 1963.

Talbot K, Mandel ID, Chilton NW: Reduction of baseline gingivitis scores with repeated prophylaxes. *J Prev Dent* 4:28-29, 1977.

Tooth	32	31
Facial Surface Score		

← MESIAL GINGIVITIS SCORE

← MIDDLE GINGIVITIS SCORE

← DISTAL GINGIVITIS SCORE

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**A Clinical Investigation of the Efficacy of Two
Dentifrices Colgate Sensitive Multi Protection
Toothpaste (Lower RDA) [PIM# 407960] and
Sensodyne Total Care F Toothpaste [PIM# 415672])
for the Reduction of Dentinal Hypersensitivity**

Protocol No. CRO-0907-SEN-RDA-YPZ

**An Eight-Week Study on Adults in
Chengdu, China**

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Howard M. Proskin & Associates, Inc.
Rochester, New York

DATES OF STUDY: October – December, 2007

DATE OF REPORT: March, 2008

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ABSTRACT

The objective of this independent, double-blind, eight-week clinical study was to investigate the efficacy of dentifrice containing 5% potassium nitrate and 1.1% sodium monofluorophosphate in a lower RDA silica base (Colgate-Palmolive Co., New York, NY) and a commercially available desensitizing dentifrice (Sensodyne Total Care F Toothpaste, GlaxoSmithKline, UK) with respect to the comparison of dentinal hypersensitivity scores.

Prospective adult male and female subjects from the Chengdu, China area reported to the clinical facility after having refrained from all oral hygiene procedures and chewing gum for eight hours, and having refrained from eating and drinking for four hours. Qualifying subjects who presented with a tactile sensitivity score (Yeaple Probe) between 10 and 50 grams of force, and an air blast sensitivity score of 2 or 3 (Schiff Cold Air Sensitivity Scale) were stratified according to their sensitivity scores and randomly assigned within strata to one of two treatment groups. The two treatment groups were: (1) a dentifrice containing 5% potassium nitrate and 1.1% sodium monofluorophosphate (Test Dentifrice with Lower RDA), and (2) a commercially available desensitizing dentifrice (Control Dentifrice). Subjects were provided with their assigned dentifrice, which was packaged in white overwrapping, and an adult soft-bristled toothbrush, and instructed to brush their teeth for one minute, twice daily, using only the dentifrice provided. Subjects returned to the testing facility after four and eight weeks of product use, having refrained from all oral hygiene procedures and chewing gum for eight hours, and from eating and drinking for four hours, prior to each follow-up visit. Assessments of tactile sensitivity and air blast sensitivity, and examinations of oral soft and hard tissue were repeated at each examination.

Eighty (80) subjects complied with the protocol, and completed the eight-week study. At the four-week and the eight-week examinations, both the Test Dentifrice with Lower RDA group and the Control Dentifrice group exhibited statistically significant improvements from baseline with respect to tactile sensitivity scores and air blast sensitivity scores.

At both the four-week and the eight-week examinations, no statistically significant difference was indicated between the Test Dentifrice with Lower RDA group and the Control Dentifrice group with respect to tactile sensitivity scores or air blast sensitivity scores.

The results of this double-blind clinical study support the conclusions that a dentifrice containing 5% potassium nitrate and 1.1% sodium monofluorophosphate in a lower silica base provides a significant reduction in dentinal hypersensitivity when used over a period of eight weeks. The dentifrice containing 5% potassium nitrate and 1.1% sodium monofluorophosphate in a lower silica base provides a level of control of dentinal hypersensitivity that does not differ significantly from that of a commercially available desensitizing dentifrice, when used over a period of eight weeks.



INTRODUCTION

The objective of this independent, double-blind, eight-week clinical study was to investigate the efficacy of a dentifrice containing 5% potassium nitrate and 1.1% sodium monofluorophosphate in a lower RDA silica base (Colgate-Palmolive Co., New York, NY) and a commercially available desensitizing dentifrice (GlaxoSmithKline, UK) with respect to the comparison of dentinal hypersensitivity scores.

MATERIALS AND METHODS

This clinical study employed a double-blind, two-treatment, parallel-groups design. Adult male and female subjects from the Chengdu, China area were enrolled in the study based upon the following criteria:

- (i) Subjects had to be between the ages of 18 and 70 (inclusive), and in generally good health.
- (ii) Subjects were required to possess a minimum of two sensitive teeth which were anterior to the molars and demonstrated cervical erosion/abrasion or gingival recession; and for which a tactile sensitivity stimuli score of 10 to 50 grams of force (Yeaple Probe) and an air blast stimuli score of 2 or 3 (Schiff Cold Air Sensitivity Scale) were presented at the baseline examination.
- (iii) Subjects were required to be available for the eight-week duration of the study, and to sign an informed consent form.
- (iv) Subjects were excluded from the study if they had gross oral pathology, chronic disease, advanced periodontal disease, treatment for periodontal disease (within the last 12 months), or sensitive teeth with a mobility greater than one. Subjects with teeth that had extensive/defective restorations (including prosthetic crowns), suspected pulpitis, caries, cracked enamel, or that were used as abutments for removable partial dentures were also excluded from the study.
- (v) Subjects were excluded from the study if they were current users of anticonvulsants, antihistamines, antidepressants, sedatives, tranquilizers, anti-inflammatory drugs or daily analgesics.
- (vi) Pregnant or lactating women, individuals who were participating in any other clinical study or who had participated in a desensitizing dentifrice study or who used a desensitizing dentifrice within the last three months, were not allowed to participate in the study.

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- (vii) Subjects with a history of allergy to the test products, or allergies to oral care/personal care consumer products or their ingredients, or subjects with existing medical conditions, which precluded them from not eating and drinking for periods up to four hours, were also excluded from the study.

Prospective study subjects reported to the clinical facility having refrained from all oral hygiene procedures and chewing gum for eight hours, and having refrained from eating and drinking for four hours prior to their examination. All prospective subjects who met the inclusion/exclusion criteria and signed an informed consent form received a baseline tactile sensitivity and an air blast sensitivity evaluation, along with an oral soft and hard tissue assessment.

For each subject who qualified for participation in the study, two sensitive teeth that satisfied the tactile and air blast sensitivity enrollment criteria were identified for evaluation throughout the study. Qualifying subjects were stratified based on baseline tactile and air blast sensitivity scores and randomly assigned within strata to one of the two study treatments:

Test Dentifrice with Lower RDA	Dentifrice containing 5% potassium nitrate and 1.1% sodium monofluorophosphate in a lower RDA silica base (Colgate-Palmolive Co., New York, NY).
Control Dentifrice	Commercially available desensitizing dentifrice (GlaxoSmithKline, UK).

Following study treatment assignment, subjects were provided with their assigned dentifrice and an adult soft-bristled toothbrush for home use. Both of the dentifrice products were supplied in their original packaging and overwrapped with a white label to mask the products' identity. Subjects were instructed to brush their teeth for one minute, twice daily, using only the dentifrice and toothbrush provided, and to refrain from any other oral hygiene procedures throughout the duration of the study. Subjects were also instructed to refrain from all oral hygiene procedures and chewing gum for eight hours, and eating and drinking for four hours prior to each follow-up examination. There were no other restrictions regarding diet or smoking habits during the course of the study.

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After four weeks, and again after eight weeks of product use, subjects returned to the clinical facility for tactile and air blast sensitivity evaluations of their baseline-designated study teeth, and for oral soft and hard tissue assessments. All examinations were performed by the same dental examiner, using the same procedures as employed at baseline. Subjects were also interviewed with respect to the presence of adverse events and the use of concomitant medications.

CLINICAL SCORING PROCEDURES

Tactile Sensitivity Assessment

Tactile sensitivity was assessed by use of the Model 200A Electronic Force Sensing Probe developed by Yeaple Research of Pittsford, NY. The application of this probe for dental sensitivity testing utilizing a #19 explorer tip at a pre-set force measured in grams was employed.

Teeth were evaluated for tactile sensitivity^{1, 2} in the following manner:

- 1) The subject was instructed to respond at the point where he/she first experienced discomfort.
- 2) The explorer tip of the probe was applied to the buccal surface of each sensitive tooth at the CEJ.
- 3) The explorer tip was stroked perpendicular to the tooth beginning at a pre-set force of 10 grams and increased by 10 gram increments until the subject experienced discomfort, or until 50 grams of force was applied.

Subjectwise scores were calculated by averaging the values measured on the two baseline-designated study teeth.

Air Blast Sensitivity Assessment

Teeth were evaluated for air blast sensitivity in the following manner:

- 1) The sensitive tooth was isolated from the adjacent teeth (mesial and distal) by the placement of the examiner's fingers over the adjacent teeth.
- 2) Air was delivered from a standard dental unit air syringe at 60 psi (± 5 psi) and 70°F ($\pm 3^\circ\text{F}$). The air was directed at the exposed buccal surface of the sensitive tooth for one second from a distance of approximately 1 cm.

- 3) The Schiff Cold Air Sensitivity Scale³ was used to assess subject response to this stimulus. This scale is scored as follows:

- 0 - Subject does not respond to air stimulus;
- 1 - Subject responds to air stimulus but does not request discontinuation of stimulus;
- 2 - Subject responds to air stimulus and requests discontinuation or moves from stimulus;
- 3 - Subject responds to air stimulus, considers stimulus to be painful, and requests discontinuation of the stimulus.

Subjectwise scores were calculated by averaging the values obtained from the two baseline-designated study teeth.

Oral Soft and Hard Tissue Assessment

The dental examiner visually examined the oral cavity and peri-oral area using a dental light and dental mirror. This examination included an evaluation of the soft and hard palate, gingival mucosa, buccal mucosa, mucogingival fold areas, tongue, sublingual and submandibular areas, salivary glands, and the tonsillar and pharyngeal areas.

Adverse Events

Adverse events were obtained from an interview with the subject, and from a dental examination by the investigator.

STATISTICAL METHODS

Statistical analyses were performed separately for the tactile sensitivity assessments and the air blast sensitivity assessments. Comparisons of the treatment groups with respect to age, and with respect to baseline tactile sensitivity and air blast sensitivity scores were performed using analyses of variance (ANOVA's). Comparisons between the treatment groups with respect to gender were performed using chi-squared tests. Within-treatment comparisons of the baseline versus follow-up tactile sensitivity and air blast sensitivity scores were performed using paired t-tests. Comparisons of the treatment groups with respect to baseline-adjusted tactile sensitivity and air blast sensitivity scores at the follow-up examinations were performed using analyses of covariance (ANCOVA's). All statistical tests of hypotheses were two sided, and employed a level of significance of $\alpha=0.05$.

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RESULTS

All of the eighty (80) subjects who entered the study complied with the protocol, and completed the eight-week examination. A summary of the gender and age of the study population is presented in Table 1. The treatment groups did not differ significantly with respect to either of these characteristics. Throughout the study, no adverse effects on the oral soft or hard tissues of the oral cavity were observed by the examiner, or reported by the subjects when questioned.

Baseline Data

Table 2 presents a summary of the tactile and air blast sensitivity scores measured at the baseline examination. For tactile sensitivity, the mean baseline scores were 19.50 for the Test Dentifrice with Lower RDA group, and 19.17 for the Control Dentifrice group. For air blast sensitivity, the mean baseline scores were 2.52 for the Test Dentifrice with Lower RDA group, and 2.53 for the Control Dentifrice group. No statistically significant difference was indicated between the treatment groups with respect to either sensitivity score at baseline.

Four-Week Data

Tactile Sensitivity

Table 3 presents a summary of the tactile sensitivity scores measured after four weeks of product use.

Comparisons versus baseline: The mean four-week tactile sensitivity scores were 40.79 for the Test Dentifrice with Lower RDA group, and 41.42 for the Control Dentifrice group. The percent changes from baseline were 109.2% for the Test Dentifrice with Lower RDA group, and 116.1% for the Control Dentifrice group, both of which were statistically significant.

Comparison between treatment groups: There was no statistically significant difference indicated between the treatment groups with respect to tactile sensitivity scores after four weeks of product use.

Air Blast Sensitivity

Table 4 presents a summary of the air blast sensitivity scores measured after four weeks of product use.

Comparisons versus baseline: The mean four-week air blast sensitivity scores were 1.70 for

the Test Dentifrice with Lower RDA group, and 1.68 for the Control Dentifrice group. The mean percent reductions from baseline were 32.5% for the Test Dentifrice with Lower RDA group, and 33.6% for the Control Dentifrice group, both of which were statistically significant.

Comparison between treatment groups: There was no statistically significant difference indicated between the treatment groups with respect to air blast sensitivity scores after four weeks of product use.

Eight-Week Data

Tactile Sensitivity

Table 5 presents a summary of the tactile sensitivity scores measured after eight weeks of product use.

Comparisons versus baseline: The mean eight-week tactile sensitivity scores were 49.38 for the Test Dentifrice with Lower RDA group, and 48.88 for the Control Dentifrice group. The mean percent changes from baseline were 153.2% for the Test Dentifrice with Lower RDA group, and 155.0% for the Control Dentifrice group, both of which were statistically significant.

Comparison between treatment groups: There was no statistically significant difference indicated between the treatment groups with respect to tactile sensitivity scores after eight weeks of product use.

Air Blast Sensitivity

Table 6 presents a summary of the air blast sensitivity scores measured after eight weeks of product use.

Comparisons versus baseline: The mean eight-week air blast sensitivity scores were 1.18 for the Test Dentifrice with Lower RDA group, and 1.08 for the Control Dentifrice group. The mean percent reductions from baseline were 53.2% for the Test Dentifrice with Lower RDA group, and 57.3% for the Control Dentifrice group, both of which were statistically significant.

Comparison between treatment groups: There was no statistically significant difference indicated between the treatment groups with respect to air blast sensitivity scores after eight weeks of product use.

Adverse Events

No significant adverse events were noted during this study.

OVERALL FINDINGS AND CONCLUSION

This double-blind clinical study provided an investigation of the efficacy of two dentifrices with respect to the dentinal hypersensitivity scores over an eight-week period.

At both the four-week and eight-week examinations, subjects in the Test Dentifrice with Lower RDA group exhibited statistically significant improvements in tactile sensitivity scores (109.2% and 153.2%, respectively). Additionally, at both the four-week and eight-week examinations, the Test Dentifrice with Lower RDA group also exhibited statistically significant reductions in air blast sensitivity scores (32.5% and 53.2%, respectively).

At both the four-week and eight-week examinations, subjects in the Control Dentifrice group exhibited statistically significant improvements in tactile sensitivity scores (116.1% and 155.0%, respectively). Additionally, at both the four-week and eight-week examinations, the Control Dentifrice group also exhibited statistically significant reductions in air blast sensitivity scores (33.6% and 57.3%, respectively).

After four weeks and again after eight weeks of product use, no statistically significant difference was indicated between the Test Dentifrice with Lower RDA group and the Control Dentifrice group with respect to tactile sensitivity scores or air blast sensitivity scores.

The results of this double-blind clinical study support the conclusions that (i) Colgate Sensitive Multi Protection Toothpaste (Lower RDA), containing 5% potassium nitrate and 1.1% sodium monofluorophosphate in a silica base, provides a significant reduction in dentinal hypersensitivity when used over a period of eight weeks; and (ii) Colgate Sensitive Multi Protection Toothpaste (Lower RDA), containing 5% potassium nitrate and 1.1% sodium monofluorophosphate in a silica base, provides a level of control of dentinal hypersensitivity that does not differ significantly from that of Sensodyne Total Care F Toothpaste, when used over a period of eight weeks.

The results of this double-blind clinical study support the conclusions that (i) Colgate Sensitive Multi Protection Toothpaste (Lower RDA), containing 5% potassium nitrate and 1.1% sodium monofluorophosphate in a silica base, provides a significant reduction in dentinal hypersensitivity when used over a period of eight weeks; and (ii) Colgate Sensitive Multi Protection Toothpaste (Lower RDA), containing 5% potassium nitrate and 1.1% sodium monofluorophosphate in a silica base, provides a level of control of dentinal hypersensitivity that does not differ significantly from that of Sensodyne Total Care F Toothpaste, when used over a period of eight weeks.

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1. Clark GE, Troullos ES: Designing hypersensitivity studies. *Dent Clin North Am* 34: 531-543, 1990.
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3. Schiff T *et al.*: Efficacy of a dentifrice containing potassium nitrate, soluble pyrophosphate, PVM/MA copolymer, and sodium fluoride on dentinal hypersensitivity: A twelve-week clinical study. *J. Clin Dent* 5 (Spec Iss): 87-92, 1994.

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STUDY SPONSOR

This clinical study was sponsored by the Colgate-Palmolive Company.

Study Director: William DeVizio, DMD

Study Monitor: Yun Po Zhang, PhD

Identification of Tested Products:

**Test Dentifrice
with Lower RDA**

Dentifrice containing 5% potassium nitrate and 1.1% sodium monofluorophosphate in a lower RDA silica base (Colgate-Palmolive Co., New York, NY).

**Control
Dentifrice**

Commercially available desensitizing dentifrice (GlaxoSmithKline, UK).

Table 1

Summary of Gender and Age

For Subjects Who Completed the Eight-Week Clinical Study

Treatment	Number of Subjects			Age	
	Male	Female	Total	Mean	Range
Test Dentifrice with Lower RDA ¹	17	23	40	53.73	26-65
Control Dentifrice ²	16	24	40	53.45	36-69

¹ Dentifrice containing 5% potassium nitrate and 1.1% sodium monofluorophosphate in a lower RDA silica base (Colgate-Palmolive Co., New York, NY).

² Commercially available desensitizing dentifrice (GlaxoSmithKline, UK).

Table 2

Summary of the **Baseline** Tactile and Air Blast Sensitivity Scores
For Subjects Who Completed the Eight-Week Clinical Study

Parameter	Treatment	n	Baseline Summary (Mean ± S.D.) ³
Tactile Sensitivity	Test Dentifrice with Lower RDA ¹	40	19.50 ± 5.00
	Control Dentifrice ²	40	19.17 ± 4.62
Air Blast Sensitivity	Test Dentifrice with Lower RDA ¹	40	2.52 ± 0.40
	Control Dentifrice ²	40	2.53 ± 0.36

- ¹ Dentifrice containing 5% potassium nitrate and 1.1% sodium monofluorophosphate in a lower RDA silica base (Colgate-Palmolive Co., New York, NY).
- ² Commercially available desensitizing dentifrice (GlaxoSmithKline, UK).
- ³ No statistically significant difference was indicated between the two treatment groups at baseline with respect to either tactile sensitivity, or air blast sensitivity.

Table 3

Summary of the **Four-Week** Tactile Sensitivity Scores
For Subjects Who Completed the Eight-Week Clinical Study

Treatment	n	Four-Week Summary (Mean ± S.D.)	Within-Treatment Analysis		Between-Treatment Comparison	
			Percent Change ³	Sig. ⁴	Percent Difference ⁵	Sig. ⁶
Test Dentifrice with Lower RDA ¹	40	40.79 ± 6.52	109.2%	p<0.05	-1.5%	NS
Control Dentifrice ²	40	41.42 ± 4.93	116.1%	p<0.05		

- ¹ Dentifrice containing 5% potassium nitrate and 1.1% sodium monofluorophosphate in a lower RDA silica base (Colgate-Palmolive Co., New York, NY).
- ² Commercially available desensitizing dentifrice (GlaxoSmithKline, UK).
- ³ Percent change exhibited by the four-week mean relative to the baseline mean. A positive value indicates an improvement in tactile sensitivity at the four-week examination.
- ⁴ Significance of paired t-test comparing the baseline and four-week examinations.
- ⁵ Difference between four-week means expressed as a percentage of the four-week mean for the Control Dentifrice. A positive value indicates an improvement in tactile sensitivity for the Test Dentifrice with Lower RDA relative to the Control Dentifrice.
- ⁶ Significance of ANCOVA comparison of baseline-adjusted means.

Table 4

Summary of the **Four-Week** Air Blast Sensitivity Scores
For Subjects Who Completed the Eight-Week Clinical Study

Treatment	n	Four-Week Summary (Mean ± S.D.)	Within-Treatment Analysis		Between-Treatment Comparison	
			Percent Reduction ³	Sig. ⁴	Percent Difference ⁵	Sig. ⁶
Test Dentifrice with Lower RDA ¹	40	1.70 ± 0.28	32.5%	p<0.05	1.2%	NS
Control Dentifrice ²	40	1.68 ± 0.33	33.6%	p<0.05		

¹ Dentifrice containing 5% potassium nitrate and 1.1% sodium monofluorophosphate in a lower RDA silica base (Colgate-Palmolive Co., New York, NY).

² Commercially available desensitizing dentifrice (GlaxoSmithKline, UK).

³ Percent reduction exhibited by the four-week mean relative to the baseline mean. A positive value indicates a reduction in air blast sensitivity at the four-week examination.

⁴ Significance of paired t-test comparing the baseline and four-week examinations.

⁵ Difference between four-week means expressed as a percentage of the four-week mean for the Control Dentifrice. A positive value indicates a reduction in air blast sensitivity for the Test Dentifrice with Lower RDA relative to the Control Dentifrice.

⁶ Significance of ANCOVA comparison of baseline-adjusted means.

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Table 5

Summary of the **Eight-Week** Tactile Sensitivity Scores
For Subjects Who Completed the Eight-Week Clinical Study

Treatment	n	Eight-Week Summary (Mean ± S.D.)	Within-Treatment Analysis		Between-Treatment Comparison	
			Percent Change ³	Sig. ⁴	Percent Difference ⁵	Sig. ⁶
Test Dentifrice with Lower RDA ¹	40	49.38 ± 6.01	153.2%	p<0.05	1.0%	NS
Control Dentifrice ²	40	48.88 ± 2.40	155.0%	p<0.05		

- ¹ Dentifrice containing 5% potassium nitrate and 1.1% sodium monofluorophosphate in a lower RDA silica base (Colgate-Palmolive Co., New York, NY).
- ² Commercially available desensitizing dentifrice (GlaxoSmithKline, UK).
- ³ Percent change exhibited by the eight-week mean relative to the baseline mean. A positive value indicates an improvement in tactile sensitivity at the eight-week examination.
- ⁴ Significance of paired t-test comparing the baseline and eight-week examinations.
- ⁵ Difference between eight-week means expressed as a percentage of the eight-week mean for the Control Dentifrice. A positive value indicates an improvement in tactile sensitivity for the Test Dentifrice with Lower RDA relative to the Control Dentifrice.
- ⁶ Significance of ANCOVA comparison of baseline-adjusted means.

Table 6

Summary of the **Eight-Week** Air Blast Sensitivity Scores
For Subjects Who Completed the Eight-Week Clinical Study

Treatment	n	Eight-Week Summary (Mean ± S.D.)	Within-Treatment Analysis		Between-Treatment Comparison	
			Percent Reduction ³	Sig. ⁴	Percent Difference ⁵	Sig. ⁶
Test Dentifrice with Lower RDA ¹	40	1.18 ± 0.29	53.2%	p<0.05	9.3%	NS
Control Dentifrice ²	40	1.08 ± 0.40	57.3%	p<0.05		

- ¹ Dentifrice containing 5% potassium nitrate and 1.1% sodium monofluorophosphate in a lower RDA silica base (Colgate-Palmolive Co., New York, NY).
- ² Commercially available desensitizing dentifrice (GlaxoSmithKline, UK).
- ³ Percent reduction exhibited by the eight-week mean relative to the baseline mean. A positive value indicates a reduction in air blast sensitivity at the eight-week examination.
- ⁴ Significance of paired t-test comparing the baseline and eight-week examinations.
- ⁵ Difference between eight-week means expressed as a percentage of the eight-week mean for the Control Dentifrice. A positive value indicates a reduction in air blast sensitivity for the Test Dentifrice with Lower RDA relative to the Control Dentifrice.
- ⁶ Significance of ANCOVA comparison of baseline-adjusted means.

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STUDY FORMULATIONS

Table 1. Colgate Sensitive Complete Care Toothpaste (PIM #407960)

Ingredient	% W/W
Water	36.7256
Sorbitol	19.7876
Hydrated Silica	13.3890
Glycerin	9.9500
Potassium Nitrate	5.1183
PEG-12	3.0000
Tetrapotassium pyrophosphate	2.4400
Zinc Citrate	2.0000
Methyl Vinyl Ether-Maleic Acid Copolymer (PVM/MA Copolymer)	1.5180
Sodium Lauryl Sulfate	1.4625
Sodium Monofluorophosphate	1.0450
Spearmint Flavor	1.0000
Potassium Hydroxide	0.7000
Cellulose Gum	0.5970
Titanium Dioxide	0.5000
Sodium Sulfate	0.3120
Sodium Saccharin	0.2550
Xanthan Gum	0.1770
Balance	0.0140
Sodium Chloride	0.0115
Unsulfated Alcohol	0.0045

*Potassium nitrate was not considered an active for purposes of this study

Table 2. Sensodyne Total Care Toothpaste (PIM #425672) Actives Only

Ingredient	% W/W
Sodium Fluoride	1450 ppm
Potassium Nitrate	5.0%