SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

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División de Nuevas Creaciones

PCT

SOLICITUD

PATENTE DE INVENCION

FASE NACIONAL

21. **EXPEDIENTE No.** 02-79084

54 **TITULO** COMPOSICION DENTIFRICA DE COMPONENTE DUAL PARA FLUORIZAR LOS DIENTES

51 **CLASIFICACION INTERNACIONAL** A61K 7/18

71 **SOLICITANTE** COLGATE - PALMOLIVE COMPANY

DOMICILIO NEW YORK, NEW YORK, ESTADOS UNIDOS DE AMERICA

74 **APODERADO** RAMIRO CASTRO DUQUE

22 **SANTAFE DE BOGOTA, D.C.**

ITORIO

02 079084 00

Industria y Comercio
SUPERINTENDENCIA

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Dependencia: 2020 DIVISION DE NUEVAS CREACIONES

FORMULARIO ÚNICO DE SOLICITUD DE PATENTE

PCT

ENTRADA EN FASE NACIONAL

1 SOLICITUD DE:

☒ Patente de Invención. ☐ Patente de Modelo de Utilidad.

☒ Capítulo I. ☐ Capítulo II.

2 SOLICITANTE (71)	Nombre: **COLGATE – PALMOLIVE COMPANY** Dirección: 300 Park Avenue, New York, NY 10022 Nacionalidad o Domicilio: Estados Unidos Lugar de Constitución: Estados Unidos Teléfono: Fax: E-mail	**IDENTIFICACION** C.C. ☐ NIT ☐ C.E. ☐ Otro ☐ Cual_____ Número
3 REPRESENTANTE O APODERADO	Nombre: RAMIRO CASTRO DUQUE Dirección: Cra. 7 No. 16-56 Piso 9 Teléfono: 380-2200 Fax: 380-2700 E-mail:	**IDENTIFICACION** C.C. ☒ NIT ☐ C.E. ☐ Otro ☐ Cual_____ Número 170.322 TP 1003
4 INVENTOR (ES) (72)	Nombre: Marilou T. Joziak, Edward A. Tavss, Steven W. Fisher, Robert J. Gambogi Dirección: 51 Burton Avenue, South River, NJ 08882; 17 Kathy Street, Kendall Park, NJ 08824; 321 Decatur Avenue, Middlesex, NJ 08846; 28 Matrick Court, Belle Mead, NJ 08502, Estados Unidos de América (Respectivamente) Nacionalidad o Domicilio: Estados Unidos de América	

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6 Título (54): COMPOSICIÓN DENTÍFRICA DE COMPONENTE DUAL PARA FLUORIZAR LOS DIENTES

7 Clasificación Internacional (51) A 61K 7/18

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Instrucciones para el diligenciamiento del presente formulario, ver reverso de esta página.

2020-F06 (01-11-15)

10 ANEXOS

- [x] Comprobante de pago de la tasa de presentación de la solicitud. $378.000
- [x] Comprobante de pago por reivindicación de prioridad. $106.000
- [ ] Documento que acredita la existencia y representación legal cuando el solicitante sea persona jurídica.
- [x] Poderes, si fuere el caso. Protocolo No. 131
- [ ] Documento de cesión del inventor al solicitante o a su causante.
- [ ] Declaraciones
- [x] Copia de la solicitud internacional. (Resumen, descripción, reivindicaciones, dibujos)
- [x] Traducción de la solicitud internacional al castellano. (Resumen, descripción, reivindicaciones, dibujos)
- [x] Copia del examen preliminar efectuado por la IPEA.
- [ ] Traducción del examen preliminar efectuado por la IPEA.
- [ ] De ser el caso, copia del contrato de acceso.
- [ ] De ser el caso, documento que acredite la licencia o autorización de uso de conocimientos tradicionales de las comunidades indígenas.
- [ ] De ser el caso, certificado de depósito del material biológico.
- [ ] Arte final 12x12.
- [ ] De ser el caso, información sobre otras solicitudes de patente o títulos obtenidos en el extranjero por el mismo titular o su causante, relacionadas parcial o totalmente con la invención de esta solicitud.
- [ ] Otros

11 FIGURA CARACTERÍSTICA:

12 Solicito la concesión de la patente,

NOMBRE: RAMIRO CASTRO DUQUE

FIRMA: _____

C.C. 170.322 de Bogotá T.P. 1003 del C.S.J.

Instrucciones para la presentación de los anexos, ver reverso de esta página.

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RECIBO OFICIAL DE CAJA 02 - 49 723
FECHA JULIO 26 DE 2002

***** C O N S I G N A C I O N *****

DEPOSITANTE	TIPO PAGO	BANCO	CUENTA	No PAGO	FECHA PGO	Vr PAGO
BRIGARD & CASTRO LTDA	CONSIGNACION	BANCO POPULAR	050-00110-6	5735334	26/07/2002	4,390 000 00

***** C O N C E P T O *****

CANT	RENTISTICO	CONCEPTO	TOTAL CONCEPTO
1	50005-01-01 SOLICITUDES	82 INVOCACION DE UNA PRIORIDAD EN NU	106 000 00
		TOTAL : $	106,000 00

SON CIENTO SEIS MIL PESOS

RESPONSABLE _____

RECIBO DE CAJA APLICADO AL EXPEDIENTE No _____

Industria y Com rcio

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Dependencia: 2020 DIVISION DE NUEVAS CREACIONES

NIT 800176089-2

RECIBO OFICIAL DE CAJA 02 - 54 664
FECHA : AGOSTO 20 DE 2002

***** C O N S I G N A C I O N *****

DEPOSITANTE	TIPO PAGO	BANCO	CUENTA	No PAGO	FECHA PGO	Vr PAGO
BRIGARD & CASTRO LTDA	CONSIGNACION	BANCO POPULAR	050-00110-6	1322872	20/08/2002	10,794 000 00

***** C O N C E P T O *****

CANT	RENTISTICO	CONCEPTO	TOTAL CONCEPTO
1	50005-01-01 SOLICITUDES	1 TRAMITES DE SOL DE PATENTE DE IN	378,000 00
		TOTAL : $	378,000 00

SON TRESCIENTOS SETENTA Y OCHO MIL PESOS

RESPONSABLE _____

RECIBO DE CAJA APLICADO AL EXPEDIENTE No _____

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COMPOSICIÓN DENTÍFRICA DE COMPONENTE DUAL PARA FLÚORIZAR LOS DIENTES

Antecedentes de la Invención

1 Campo de la Invención

Esta invención está dirigida a una composición dentífrica que contiene compuestos de fluoruro acidulados efectivos como agentes anti-caries y mas particularmente a una composición dentífrica de componente dual de fluoruro de fosfato acidulado para fluorizar los dientes

2 El Arte Previo

Se ha conocido durante largo tiempo incluir compuestos que contienen fluoruro en dentífricos como agentes anti-caries, y se ha establecido que estos compuestos son efectivos en reducir la incidencia de la caries dental Los compuestos de fluoruro que son considerados como los más efectivos son el fluoruro de sodio, el monofluorofosfato de sodio y el fluoruro estanoso Los compuestos de fluoruro son efectivos principalmente debido a los iones de fluoruro los cuales mejoran la resistencia ácida del esmalte dental y aceleran la re-mineralización (es decir la re-calcificación) de los dientes débiles en su etapa temprana cuando la descalcificación ha procedido solo ligeramente El efecto de mejorar la resistencia ácida del esmalte se considera debido al hecho de que los iones de fluoruro son incorporados dentro de una rejilla de cristal de hidroxiapatita que es el principal constituyente del esmalte dental o, en otras palabras, los iones de fluoruro fluorizan parcialmente la hidroxiapatita y reparan simultáneamente las irregularidades de la rejilla

La efectividad del tratamiento de fluoruro en proporcionar resistencia ácida al esmalte dental depende de la cantidad de ión de fluoruro que esta disponible para la deposición en el esmalte que se está tratando Además, usando NaF amortiguado de fosfato, la incorporación de flúor como CaF_2 en el esmalte dental se facilita a bajos niveles de pH lo cual incrementa la solubilidad del esmalte Prencipe y otros, Coloide & Quimica de Superficie, 4to Congreso Quimico de America, NY (Agosto 25 a 30, 1991) Es, consecuentemente, deseable formular un dentífrico de fluor de fosfato acidulado para mejorar la deposición de fluor hacia y toma dentro del esmalte dental

El fluoruro de fosfato acidulado se divulga en las Patentes de los Estados Unidos 4,080,440 y 5,603,992 como suministrado en un dentifrico de componente dual que comprende un primer componente acídico envasado separadamente que contiene una sal de fluoruro tal como NaF, la cual con un segundo componente que contiene ión de calcio catiónico envasado separadamente, forma el dentifrico de dos componentes para la re-mineralizacion de los dientes Aunque estoas formulaciones de dos componentes envasadas separadamente evitan cualesquiera reacciones entre ingredientes dentro del primer y segundo componentes durante el almacenamiento, ante la aplicación a los dientes la sal de fluoruro comenzará a reaccionar con el ion de calcio catiónico, reduciendo la disponibilidad de fluoruro para fluorización de los dientes Adicionalmente, una reacción ocurre durante el almacenamiento dentro del mismo primer componente, entre el ácido, el fluoruro de sodio y el abrasivo de sílice dentro de él, reduciendo la biodisponibilidad del ión de fluoruro El ingrediente abrasivo de sílice amorfa generalmente usado en dentifricos es uno de los abrasivos disponibles más químicamente inertes, sin embargo, los átomos de oxígeno cargados negativamente de la sílice son protonados en el ambiente ácido, y el hidrogeno de las fracciones

resultantes de hidroxilo (OH) se enlazan a los iones de fluoruro disponibles liberados del fluoruro de sodio Este enlace de fluoruro-OH ocurre en los sistemas de abrasivo de sílice de fluoruro de fosfato acidulado divulgados en las Patentes del arte previo 4,080,440, y 5603,922 por lo cual, la disponibilidad de los iones de fluoruro presentes en el dentífrico para fluorizar el esmalte ante su aplicación se reduce significativamente La magnitud de esta reducción en fluoruro disponible se demuestra aquí posteriormente

Consecuentemente, existe una clara necesidad de formular un dentífrico estable de fluoruro de fosfato acidulado, que tiene el fluoruro máximo suministrable

RESUMEN DE LA INVENCIÓN

De acuerdo con la presente invención se proporciona un método para fluorizar el esmalte dental usando un dentífrico de multiples componentes que comprende dos componentes acuosos semi-sólidos envasados separadamente, el primer componente que contiene fluoruro de sodio como una fuente de iones de fluoruro, en un vehículo oralmente aceptable que tiene un pH de por lo menos alrededor de 7,5 y, el segundo componente el cual está libre de fluoruro que contiene tanto una fuente de iones de fosfato como un acido para proporcionar un pH de desde alrededor de 2,5 hasta alrededor de 5,0, en un vehiculo oralmente aceptable, cada componente que contiene un abrasivo silíceo y cada componente que está libre de cualquier componente que contiene ión de calcio catiónico, tal como sales de calcio solubles en agua, por lo cual ante el mezclado de los componentes, se forma una mezcla que tiene un pH de desde alrededor de 4,0 hasta alrededor de 6,0, por lo cual ante la aplicacion de la mezcla a los dientes, la disponibilidad de iones de

fluoruro se mejora

No ha habido reconocimiento en el arte previo de la pérdida significativa de la disponibilidad de fluoruro durante periodos extendidos de almacenamiento, que resultan de la interacción de abrasivos de sílice generalmente inertes, con fluoruro de sodio, cuando el NaF está presente como la fuente de fluoruro en dentífricos que tienen un ambiente ácido De acuerdo con la presente invención, tal como se demostrará adicionalmente aquí, la mejorada disponibilidad de fluoruro que resulta de la separación del acido y el fluoruro en componentes separados del dentífrico, cada uno que contiene un abrasivo de sílice, es inesperada y significativa

Descripción de las Modalidades Preferidas

Durante el uso, los componentes del dentífrico de dos componentes de la presente invención comprenden un primer componente de dentífrico que contiene fluoruro de sodio y abrasivo de sílice, y un segundo componente de dentífrico que contiene ácido y abrasivo de sílice , estos dos componentes se combinan preferiblemente en proporciones en peso aproximadamente iguales, en forma tal que alrededor de una mitad de la concentración de cualquier ingrediente particular dentro de cualquier componente estará presente cuando los componentes se combinan y aplican a los dientes, como por cepillado Ambos componentes se formulan para proporcionar similares características físicas evidentes, en forma tal que los dos componentes son suministrados simultáneamente en las cantidades predeterminadas por extrusión desde un tubo de multiples compartimientos o dispositivo de bomba

Vehiculo Dentífrico Comun a Ambos Componentes

En la preparación de los componentes individuales del dentífrico de la presente invención, el respectivo fluoruro de sodio o ácido se incorpora dentro de un vehiculo de dentífrico adecuado para uso en la cavidad oral, el cual contiene agua, humectante, tensioactivo y un agente de pulido o abrasivo El humectante es generalmente una mezcla de humectantes, tal como glicerol, sorbitol y polietilenglicol de un peso molecular en el rango de 200 a 1 000, pero otras mezclas de humectantes y humectantes simples pueden tambien emplearse El contenido de humectante dentro de cada uno de los dos componentes está en el rango de alrededor de 20% hasta alrededor de 50% en peso y preferiblemente alrededor de 30 hasta alrededor de 45% en peso El contenido de agua es de desde alrededor de 20% hasta alrededor de 45%, y preferiblemente de alrededor de 30 hasta alrededor de 42% en peso

Agentes activos de superficie o tensioactivos pueden incorporarse en el vehículo de los componentes individuales de la presente invención, como un ingrediente para ayudar en la dispersión a todo el través del dentífrico a todo el través de la cavidad oral cuando se aplica allí, así como, para mejorar la aceptabilidad cosmética del dentífrico y las propiedades de formación de espuma Se prefieren los tensioactivos aniónicos en el primer componente que contiene fluoruro de sodio Los tensioactivos no iónicos se prefieren en el segundo componente que contiene ácido

Ejemplos de adecuados tensioactivos aniónicos para uso en el primer componente de la presente invencion incluyen sales solubles en agua de los sulfatos de alquilo superior o sulfoacetato, tal como sulfato lauril de sodio, sulfoacetato lauril de sodio u otros adecuados sulfatos de

alquilo o sulfoacetatos que tienen 8 a 18 átomos de carbono en el grupo alquilo, sales solubles en agua de mono-glicéridos sulfonatados de ácidos grasos superiores, tales como sulfonato mono-glicérido de coco de sodio y otro mono-glicérido sulfonatado adecuado de ácido graso de 10 a 18 átomos de carbono, sales de fosfato lauril de sodio de amidas de ácido graso superior, por ejemplo, ácidos de 12 a 16 átomos de carbono, con aminoacidos alifáticos inferiores, por ejemplo, taurina o sarcosina, u otro aminoácido de 2 a 6 átomos de carbono, tal como sodio-N-metil-N-palmitoil taurido, sodio N-lauroil-, N-miristoil- y N-palmitoil sarcosinatos, sales solubles en agua de los ésteres de dichos ácidos grasos con ácido isetionico o con mono-sulfato de glicerol, tal como la sal de sodio de mono-glicerido mono-sulfatado de ácidos grasos de aceite de coco hidrogenado, sales solubles en agua de sulfonatos de olefina, por ejemplo, sulfonatos de alqueno o sulfonatos de hidroxialqueno o sus mezclas que tienen 12 a 16 átomos de carbono en la cadena de carbono de la molécula, y jabones solubles en agua de acidos grasos superiores, tales como aquellos de 12 a 18 atomos de carbono, por ejemplo , ácidos grasos de coco

Ejemplos de adecuados tensioactivos no iónicos para uso en el segundo componente de la presente invención incluyen condensados de ésteres de sorbitan de ácidos grasos con oxido de etileno (polisorbatos) tal como mono-oleato de sorbitan con desde alrededor de 20 hasta alrededor de 60 moles de óxido de etileno Un polisorbato particularmente preferido es el Polisorbato 20, polioxietileno 20 mono-laurato de sorbitan, mercadeado por ICI, Newcastle, Delaware 19720

Adicionales tensioactivos no iónicos adecuados utiles en el segundo componente de la presente invención son los productos de condensación de un oxido de alfa-olefina que contiene 10 a 20 átomos de

carbono, un alcohol polihídrico que contiene 2 a 10 átomos de carbono y 2 a 6 grupos hidroxilo, y ya sea óxido de etileno o una mezcla de óxido de etileno y óxido de propileno Los tensioactivos resultantes son polímeros que tienen un peso molecular en el rango de desde alrededor de 400 hasta alrededor de 1600, contienen desde alrededor de 40% hasta alrededor de 80% de óxido de etileno, en peso, y tienen una relación molar de óxido de alfa-olefina con respecto a alcohol polihídrico en el rango de desde alrededor de 1 1 hasta alrededor de 1 3, respectivamente Otros tensioactivos no iónicos útiles en la presente invencion incluyen condensados de ésteres de sorbitan de ácidos grasos con polietilenglicol tal como diisostearato de sorbitan condensado con polietilenglicol

El agente activo de superficie puede estar presente en uno o ambos de los componentes de las composiciones de la presente invención, a una concentracion de alrededor de 0,1 hasta alrededor de 5,0% en peso, preferiblemente alrededor de 0,2 hasta alrededor de 1,5% en peso del componente particular

Materiales abrasivos de silice utiles en la práctica de la invencion incluyen, sílices preferidas que tienen un tamaño promedio de partículas de hasta alrededor de 20 micrones, incluyendo una sílice hidratada amorfa precipitada, tal como Zeodent 115, mercadeada por J M Huber Chemicals Division, Havre de Grace, Maryland 21078, o Sylodent 783 mercadeado por Grace Davidson, Baltimore, Maryland 21203

El abrasivo de silice está presente en cada uno de los dos componentes de dentífrico de la presente invención a una concentracion de desde alrededor de 5 hasta alrededor de 30% en peso, y preferiblemente alrededor de 5 hasta alrededor de 20% en peso del respectivo componente

Componente que Contiene Fuente de Fluoruro

El primer componente de la composición dentífrica de la presente invención contiene fluoruro de sodio, como la fuente de iones de fluoruro El fluoruro de sodio se incorpora en el primer componente a una concentracion de alrededor de 0,1 hasta alrededor de 3,0% en peso, y preferiblemente a alrededor de 2,0 hasta alrededor de 2,5% en peso A estas concentraciones preferidas, alrededor de 4 500 ppm hasta más de 5 600 ppm, el ion de fluoruro sera disponible en solución, cuando los primer y segundo componentes combinados de la composición dentífrica se mezclan y aplican a los dientes

Es también crítico para la práctica de la presente invención que el primer componente sea mantenido a un pH de por lo menos alrededor de 7,5, y preferiblemente a un pH de por lo menos alrededor de 8,0 Los solicitantes han descubierto que el NaF es estable en presencia del abrasivo de sílice unicamente en un ambiente de pH básico o neutral Un agente amortiguador, tal como hidróxido de sodio y bicarbonato de sodio o fosfato de sodio puede emplearse para ajustar el pH del componente de dentífrico que contiene el ión de fluoruro a los deseados niveles básicos, si es necesario

Componente que Contiene Ácido

El segundo componente de la composición dentífrica de la presente invención, el cual se mantiene separado físicamente del primer componente hasta le mezcla antes del uso, contienen un ácido o mezcla de ácidos, para acidular el dentífrico cuando los dos componentes se mezclan antes del uso Los compuestos acídicos que pueden estar presentes en el segundo componente incluyen ácidos tanto minerales

como organicos, tales como, ácido sulfurico, ácido clorhídrico, acido maleico, ácido algínico, ácido cítrico, ácido succínico, acido láctico, ácido tartárico, bitartrato de potasio, citrato de sodio ácido, ácido de fósforo, y fosfato de ácido de sodio Los fosfatos ácidos se prefieren, incluyendo ácido de fósforo, o sales de ácido de fósforo que contienen el radical PO_4, como dichos ácidos o sus sales ácidas, tales como fosfato de sodio monobasico, no solamente proporcionan la necesaria acidez, sino que también proporcionan iones de fosfato, para inhibir cualquier desmineralización del esmalte dental que puede ocurrir con la aplicación del dentífrico acidulado de dos componentes a los dientes Adicionalmente, la combinación de un ácido tal como el ácido de fosforo y una sal ácida, tal como fosfato de sodio monobásico, proporciona mejorada amortiguación para lograr el deseado pH ante la mezcla de los componentes del dentífrico El acido preferido, ácido de fósforo se encuentra comercialmente disponible como un líquido a 85% de concentración y el preferido fosfato de sodio monobásico está comercialmente disponible como un polvo de mono-hidrato

El acido se incorpora en el segundo componente de la composición dentífrica de la presente invención en una concentración total de alrededor de 0,7% hasta alrededor de 4% en peso y preferiblemente a alrededor de 2,0 hasta alrededor de 3,0% en peso, la cantidad que es suficiente para obtener un pH de desde alrededor de 2,5 hasta alrededor de 5,0 y preferiblemente desde alrededor de 3,5 hasta alrededor de 4,5

La concentración de iones de fosfato dentro del segundo componente de la presente invención es de por lo menos alrededor de 0,05 M, con una concentración de por lo menos alrededor de 0,2 M preferida

Otros Ingredientes Comunes a Ambos Componentes

Espesantes inorganicos u orgánicos pueden incluirse en ambos componentes del dentífrico de la presente invención Espesantes orgánicos tales como, gomas naturales y sintéticas y coloides pueden tambien incorporarse en la presente invención Ejemplos de dichos espesantes orgánicos incluyen carragina (mosto Irlandés), goma de xantan y carboximetil celulosa de sodio, almidón, polivinilpirrolidona, hidroxietilpropil celulosa, hidroxibutil metil celulosa, hidroxipropilmetil celulosa, y hidroxietil celulosa Los espesantes inorganicos incluyen compuestos de silice amorfa que funcionan como agentes espesantes, tales como compuestos de silices coloidales disponibles bajo nombres comerciales tales como sílice fumante Cab-o-sil fabricada por Cabot Corporation y distribuida por Lenape Chemical, Bound Brook, New Jersey, Zeodent 165 de J M Huber Chemicals Division, Havre de Grace, Maryland 21078, y Sylox 15 de Grace Davidson, Baltimore, Maryland 21203 Una combinación de agentes espesantes inorgánicos y orgánicos se prefiere y puede estar presente en ambos componentes del actual dentífrico en proporciones de alrededor de 0,5 hasta alrededor de 15% en peso, preferiblemente alrededor de 0,8 hasta alrededor de 6% en cada uno de los dos componentes del dentífrico

Un producto dentífrico en bandas puede obtenerse usando el dentífrico de multiples componentes de la presente invencion, donde colorantes de colores contrastantes se incorporan en cada uno de los componentes del dentifrico a ser dispensado, los colorantes que son no tóxicos cuando se usan en las cantidades sugeridas Los colorantes usados en la práctica de la presente invención incluyen tanto pigmentos como tintas

Los pigmentos usados en la práctica de la presente invención incluyen pigmentos no tóxicos, inorgánicos insolubles en agua tales como dióxido de titanio, (TiO_2) y verdes de óxido de cromo, azules ultramarinos y rosados y óxidos férricos Las tintas incluyen lagos de tinta insoluble en agua preparados extendiendo sales de calcio o aluminio de tintas FD&C en alumina tal como lago FD& C Verde #1, lago FD&C Azul #2, lago FD&C R&D #30 y lago FD&C # Amarillo 15 La concentración del pigmento o tinta en la composición dentífrica varía dentro del rango en una cantidad de desde alrededor de 0,0005 por ciento hasta alrededor de 2 por ciento en peso del respectivo componente

Otros ingredientes que pueden incorporarse en uno o ambos componentes de la presente invención, incluyen agentes antibacterianos, agentes, activos anti-caries, edulcorantes, sabor y preservativos, tales como benzoato de sodio

Agentes antibacterianos preferidos son los agentes antibacterianos no catiónicos basados en compuestos fenólicos y bisfenólicos, éteres difenilo halogenados tales como triclosan, esteres de benzoato y carbanilidas Los agentes antibacterianos catiónicos que se prefieren igualmente, incluyen sales de amonio cuaternario, tales como, digluconato de clorhexidina, pueden incluirse unicamente en el segundo componente que contiene ácido de la presente invención Dichos agentes antibacterianos pueden estar presentes en cantidades de desde alrededor de 0,03 hasta alrededor de 1% en peso del componente particular

Activos anti-caries tales como tripolifosfato de sodio, pirofosfatos de tetra-potasio o tetra-sodio, o sus mezclas, pueden estar presentes en concentraciones de desde alrededor de 0,5 hasta alrededor de 8% en peso del componente particular donde dichos activos son estables El

contenido de edulcorante será normalmente el de un edulcorante artificial o sintético y su normal proporción presente estara en el rango de 0,1 a 1% en peso del componente respectivo, preferiblemente 0,2 a 0,5% en peso del respectivo componente El contenido de sabor, el cual es preferiblemente una fruta o un sabor mezclado de menta/mentol, estará usualmente en el rango de 0,5 a 2% en peso del respectivo componente, preferiblemente 0,5 a 1,0% en peso del respectivo componente Los contenidos de otros componentes o adyuvantes no excederán normalmente de 10% en peso, a menudo serán de menos de 5% en peso, y pueden ser tan poco como 0%

Cuando los agentes antibacterianos no catiónicos se incluyen en cualquiera de los componentes del dentífrico, tambien se incluira preferiblemente desde alrededor de 0,05 hasta alrededor de 5% de un agente mejorador antibacteriano (AEA) el cual mejora el suministro y la retención del agente antibacteriano no catiónico a, y su retención en las superficies orales Los AEA utiles en la presente invención se divulgan en las Patentes de los Estados Unidos U S 5,188,821 y 5,192,531, e incluyen policarboxilatos polimericos aniónicos sintéticos, en forma de copolímeros 1 4 a 4 1 de anhídrido maleico o acido con otro monómero no saturado etilénicamente polimerizable, preferiblemente metil vinilo éter/anhidrido maleico que tiene un peso molecular (P M) de alrededor de 30 000 hasta alrededor de 1 000 000, más preferiblemente alrededor de 30 000 hasta alrededor de 800 000 Estos copolímeros se encuentran disponibles por ejemplo como Gantrez, por ejemplo, AN 139 (P M 500 000), AN 119 (P M 250 000) y preferiblemente S-97 Grado Farmacéutico (P M 700 000) disponible en ISP Technologies, Inc , Bound Brook, N J 08805

Preparación del Dentífrico

Para preparar cualquiera de los componentes del dentífrico de la presente invención, generalmente los humectantes por ejemplo, los ingredientes de glicerina, propilenglicol, polietilenglicol, son dispersados con cualquier edulcorante y agua en un mezclador convencional, hasta que la mezcla se vuelve una fase de gel homogenea Dentro de la fase de gel se agrega un pigmento tal como TiO_2, cualquier agente antibacteriano tal como triclosan, cualquier agente mejorador antibacteriano tal como Gantrez, cualesquiera agentes de control de caries tales como pirofosfato de tetra-sodio o tripolifosfato de sodio o ambos, en el segundo componente el fosfato acido, y en el primer componente la fuente de ión de fluoruro, es decir fluoruro de sodio Estos ingredientes se mezclan hasta que se obtiene una fase homogénea Posteriormente los ingredientes como el espesante, el abrasivo de silice, el sabor y el tensioactivo son agregados a alta velocidad bajo vacío de desde alrededor de 20 a 100 mm de Hg El producto resultante es en el caso de cada componente un producto homogéneo, semi-sólido, o pasta extruible

Empaque del Dentífrico

La composición dentífrica de multiples componentes de la presente invención se empaca en un adecuado recipiente dispensador donde los componentes son mantenidos separados fisicamente y desde los cuales los componentes separados pueden dispensarse sincronizadamente como una cinta para aplicación a un cepillo dental Dichos recipientes son conocidos en el arte Un ejemplo de un recipiente tal se un recipiente de dispensado de dos compartimientos, tal como una bomba o tubo, que tiene paredes laterales colapsables, como se divulga en las Patentes de los Estados Unidos U S 4,487,757 y 4,687,663, donde, el cuerpo del

recipiente se forma a partir de un sustrato plástico colapsable y se proporciona con una particion dentro del cuerpo del recipiente, definiendo compartimientos separados donde los componentes físicamente separados son almacenados y desde los cuales son dispensados a través de un puerto de salida de dispensado adecuado

El siguiente ejemplo es adicionalmente ilustrativo de la presente invencion, pero se entiende que la invención no está limitada a él Todas las cantidades y proporciones a las cuales se hace referencia aquí y en las reivindicaciones del apéndice estan dadas en peso, a menos que se establezca de otra forma

EJEMPLO

Un dentífrico de dos componentes de la presente invención se preparó, designado Pasta Dental I, que tienen un primer componente que contiene fluoruro de sodio y abrasivo de sílice y un segundo componente que contiene fosfato ácido y abrasivo de silice Los ingredientes y el pH de cada uno de los dos componentes de la Pasta Dental I se muestran en la Tabla 1, más abajo

Tabla I

Pasta Dental I

Ingredientes	1er componente (en % en peso)	2ndo componente (en % en peso)
PEG 600	3,00	3,00
Goma de Xantan	0,80	0,80
Sorbitol	37,15	36,58
Agua	39,24	38,24
Fluoruro de Sodio*	2,21	—
Benzoato de Sodio	0,50	0,50
Ácido Fosforico 85%	—	0,96
Fosfato de Sodio monobasico	—	1,82
Sacarosa de sodio	0,25	0,25
Tinta	0,50	0,50
Sylox 15	10,0	10,0
Zeodent 115	5,35	5,35
Polisorbato 20	—	0,50
Sulfato Lauril de Sodio	1,0	—
Sabor	0,50	0,50
Total (%)	100%	100%
pH	8,0	3,5

*Contiene potencialmente 5 000 ppm de F^- liberable con combinación de los 1er y 2ndo componentes ante la mezcla antes de la aplicación a la dentadura

Para determinar la disponibilidad del ión de fluoruro del dentífrico de multiples componentes de la presente invencion, después del almacenamiento durante un periodo de 8 semanas, los 1er y 2ndo componentes de la Pasta Dental I se mezclaron conjuntamente, diluyeron mil veces usando una solución amortiguadora comercialmente disponible (Orion TISAB II), a temperatura ambiente, la concentración del ión de fluoruro disponible se determinó usando un Analizador Corning Modelo 350 pH/ión, Corning Inc , Corning N Y, equipado con un Electrodo de Fluoruro Orion, Modelo #94-09, Orion Research Products, Boston, Mass La salida EMF del Electrodo de Fluoruro Orion se convirtió a ppm de fluoruro mediante una calibración logarítmica-lineal establecida con concentraciones conocidas de fluoruro en la solución amortiguadora y el

ppm resultante de fluoruro disponible determinado como se registra en la Tabla III, de abajo

Con propósitos de comparacion, el procedimiento se repitió excepto porque el dentifrico ensayado en cuanto a disponibilidad de fluoruro era un dentífrico de fluoruro de fosfato acidulado de un unico componente del arte previo, que contiene un abrasivo de silice designado, Pasta Dental II, que tiene los ingredientes y el pH listados en la Tabla II, de abajo Haciendo referencia a la Tabla II, notar que la cantidad del fluoruro de sodio dentro de la Pasta Dental II es la mitad de la del 1er Componente de la pasta Dental I, en forma tal que un potencial comparable de 5 000 ppm de fluoruro puede suministrarse ante el uso por cada uno Después de ocho semanas comparables de almacenamiento, el fluoruro soluble disponible de la Pasta Dental II se ensayó usando la misma metodología que la usada para la Pasta Dental I y los resultados se registraron en la Tabla III, de abajo

Tabla II

Pasta Dental II

Ingredientes	Composicion (en % en peso)
PEG 600	3,00
Goma de Xantan	0,80
Sorbitol	34,37
Agua	39,345
Fluoruro de Sodio	1,105
Benzoato de Sodio	0,50
Ácido Fosfórico 85%	0,96
Fosfato de Sodio monobásico	1,82
Sacarosa de sodio	0,25
Tinta	0,50
Sylox 15	10,0
Zeodent 115	5,35
Polisorbato 20	0,50
Sulfato Lauril de Sodio	1,0
Sabor	0,50
Total (%)	100%
pH	5,0

Tabla III

Disponibilidad de Fluoruro

Pasta dental analizada	Ión de Fluoruro Soluble Disponible
Pasta Dental I	4 900
Pasta Dental II	3 800

Haciendo referencia a la Tabla III, 4 900 ppm es equivalente al 98% de disponibilidad del fluoruro en la Pasta Dental I y 3 800 ppm es equivalente correspondientemente al 76% de disponibilidad del fluoruro en la Pasta Dental II La diferencia del 22% en fluoruro disponible entre la Pasta Dental I de la presente invención y la Pasta Dental II comparativa es significativa e inesperadamente grande La magnitud de la pérdida de fluoruro disponible en la Pasta Dental II está a un nivel de significación que vuelve la Pasta Dental II comercialmente inaceptable

Lo que se Reivindica es.

1 Un método para la fluorización de dientes que utiliza un sistema de dentífrico de dos componentes el cual está libre de cualesquiera sales de calcio solubles en agua que comprende los pasos de (1) preparar un primer componente dentífrico que contiene desde alrededor de 2,0% hasta alrededor de 2,5% en peso de fluoruro de sodio como la fuente de fluorización y que tiene un pH de por lo menos alrededor de 7,5, y un segundo componente de dentífrico libre de fluoruro, que contiene una fuente de iones de fosfato y un ácido en una cantidad suficiente para mantener el pH en el rango de alrededor de 2,5 hasta alrededor de 5,0, ambos componentes de dentífrico que contienen un abrasivo de sílice, (2) mantener los primer y segundo componentes de dentífrico separados el uno del otro hasta la aplicación a los dientes que requieren de fluorización, (3) mezclar los primer y segundo componentes conjuntamente para formar una mezcla que tiene un pH de desde alrededor de 4,0 hasta alrededor de 6,0, (4) aplicar la mezcla a los dientes, por lo cual se observa mejorada disponibilidad de iones de fluoruro en el esmalte dental

2 El método de la reivindicacion 1, donde la fuente de iones de fosfato es ácido fosforico, monobásico de fosfato de sodio o una combinación de ellos

3 El método de la reivindicación 1, donde el primer componente contiene desde alrededor de 0,1 hasta alrededor de 3,0% en peso de fluoruro de sodio

4 El método de la reivindicación 1, donde el segundo componente contiene desde alrededor de 0,7 hasta alrededor de 4% en peso de un fosfato ácido y una sal ácida

5 El método de la reivindicacion 4, donde el fosfato ácido es ácido fosfórico y la sal ácida es monobásica de fosfato de sodio

6 El método de la reivindicación 1, donde el pH del primer componente es por lo menos alrededor de pH 8,0

7 El metodo de la reivindicación 1, donde el ácido está en una cantidad suficiente para mantener el pH del segundo componente en el rango de alrededor de pH 3,5 hasta alrededor de pH 4,5

8 El método de la reivindicación 1, donde el abrasivo de silice es una sílice hidratada amorfa precipitada

9 El método de la reivindicación 8, donde la composición dentífrica contiene desde 10 hasta 30% en total del abrasivo de sílice amorfo hidratado

10 El metodo de la reivindicación 9, donde ambos componentes del sistema de dentífrico contienen cada uno 15,35% en peso del abrasivo de silice amorfo hidratado

11 El método de la reivindicación 1, donde un tensioactivo se incorpora en ambos componentes del sistema de dentífrico

12 El método de la reivindicación 11, donde el tensioactivo incorporado en el primer componente del sistema de dentífrico es sulfato lauril de sodio y el tensioactivo incorporado en el segundo componente del dentífrico es un condensado de ésteres de sorbitan de ácidos grasos con óxido de etileno

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(54) Title: DUAL COMPONENT DENTIFRICE COMPOSITION FOR FLUORIDATING TEETH

(57) Abstract: A method is disclosed for enhancing fluoride availability using an acidulated two component dentifrice system in which the first component contains sodium fluoride and a silica abrasive in an alkaline environment and the second component contains an acid, a phosphate ion source, and a silica abrasive.

DUAL COMPONENT DENTIFRICE COMPOSITION FOR FLUORIDATING TEETH

Background Of The Invention

1 Field of the Invention

This invention is directed to a dentifrice composition containing acidulated fluoride compounds effective as anticaries agents and more particularly to an acidulated phosphate fluoride dual component dentifrice composition for fluoridating teeth

2 The Prior Art

It has long been known to include fluoride containing compounds in dentifrices as anticaries agents, and it has been established that these compounds are effective to reduce the incidence of dental caries Fluoride compounds which are deemed to be the most effective are sodium fluoride, sodium monofluorophosphate and stannous fluoride The fluoride compounds are effective mainly due to the fluoride ions which improve the acid resistance of tooth enamel and accelerate remineralization (i e recalcification) of decayed teeth in their early stage when the decalcification has proceeded only slightly The effect of improving the acid resistance of the enamel is believed to be due to the fact that the fluoride ions are incorporated into a crystal lattice of hydroxyapatite which is the main constituent of tooth enamel or, in other words, fluoride ions partially fluoridate hydroxyapatite and simultaneously repair the lattice irregularities

The effectiveness of fluoride treatment in providing acid resistance to tooth enamel is dependent upon the amount of fluoride ion which is

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The effectiveness of fluoride treatment in providing acid resistance to tooth enamel is dependent upon the amount of fluoride ion which is

available for deposition on the enamel being treated. Also, using phosphate buffered NaF, the incorporation of fluoride as CaF_2 into dental enamel is facilitated at lower pH levels which increase enamel solubility. Prencipe et al., Colloid & Surface Chemistry, 4th Chemical Congress of America, NY (Aug. 25-30, 1991). It is, therefore, desirable to formulate an acidulated phosphate fluoride dentifrice to enhance fluoride deposition onto and uptake into the tooth enamel.

Acidulated phosphate fluoride is disclosed in U.S. Patents 4,080,440 and 5,603,992 as delivered in a dual component dentifrice comprised of a separately housed first acidic component containing a fluoride salt such as NaF, which with a second separately housed cationic calcium ion containing component, forms the two component dentifrice for tooth remineralization. While these two separately housed component formulations avoid any reactions between ingredients within the first and second components during storage, upon application to the teeth the fluoride salt will begin to react with the cationic calcium ion, reducing the availability of the fluoride for fluoridation of the teeth. Further, a reaction occurs during storage within the first component itself, between the acid, the sodium fluoride and the silica abrasive therein, reducing the bioavailability of the fluoride ion. The amorphous silica abrasive ingredient generally used in dentifrices is one of the most chemically inert abrasives available, however, the negatively charged oxygen atoms of the silica are protonated in the acid environment, and the resulting hydroxyl (OH) moieties hydrogen bond to the available fluoride ions released from the sodium fluoride. This fluoride-OH bond occurs in the acidulated phosphate fluoride silica abrasive systems disclosed in prior art Patents 4,080,440, and 5603,922 whereby, the availability of the fluoride ions present in the dentifrice to fluoridate the enamel upon application thereto is significantly reduced. The magnitude of this reduction in available fluoride is hereinafter demonstrated.

Thus, there is a clear need to formulate a stable, acidulated phosphate fluoride dentifrice, having the maximum deliverable fluoride.

SUMMARY OF THE INVENTION

In accordance with the present invention there is provided a method for the fluoridation of tooth enamel using a multicomponent dentifrice comprised of two separately housed, semi-solid aqueous components, the first component containing sodium fluoride as a source of fluoride ions, in an orally acceptable vehicle having a pH of at least about 7 5 and, the second component which is fluoride free containing both a source of phosphate ions and an acid to provide a pH of from about 2 5 to about 5 0, in an orally acceptable vehicle, each component containing a siliceous abrasive and each component being free of any cationic calcium ion containing component, such as water soluble calcium salts, whereby upon mixing of the components, a mixture having a pH of from about 4 0 to about 6 0 is formed, whereby upon application of the mixture to the teeth, the availability of fluoride ions is enhanced

There has been no recognition in the prior art of the significant loss of fluoride availability during extended periods of storage, resulting from the interaction of generally inert silica abrasives, with sodium fluoride, when NaF is present as the fluoride source in dentifrices having an acid environment. In accordance with the present invention, as will be further demonstrated herein, the enhanced fluoride availability resulting from separating the acid and the fluoride in separate dentifrice components, each containing a silica abrasive, is unexpected and significant.

Description Of The Preferred Embodiments

In use, the components of the two component dentifrice of the present invention comprise a first sodium fluoride and silica abrasive containing dentifrice component, and a second acid and silica abrasive containing dentifrice component, these two components are preferably combined in approximately equal weight proportions, so that about one-half of the concentration of any particular ingredient within either component

will be present when the components are combined and applied to the teeth, as by brushing. Both components are formulated to provide similar apparent physical characteristics, so that the two components are simultaneously delivered in the desired predetermined amounts by extrusion from a multicompartmented tube or pump device.

Dentifrice Vehicle Common to Both Components

In the preparation of the individual dentifrice components of the present invention, the respective sodium fluoride or acid is incorporated within a dentifrice vehicle suitable for use in the oral cavity, which contains water, humectant, surfactant and a polishing agent or abrasive. The humectant is generally a mixture of humectants, such as glycerol, sorbitol and polyethylene glycol of a molecular weight in the range of 200-1000, but other mixtures of humectants and single humectants may also be employed. The humectant content within each of the two components is in the range about of 20% to about 50% by weight and preferably about 30 to about 45% by weight. The water content is from about 20% to about 45%, and preferably about 30 to about 42% by weight.

Surface active agents or surfactants may be incorporated in the vehicle of the individual components of the present invention, as an ingredient to aid in the thorough dispersion of the dentifrice throughout the oral cavity when applied thereto, as well as, to improve the dentifrice's cosmetic acceptability and the foaming properties. Anionic surfactants are preferred in the first, sodium fluoride, containing component. Nonionic surfactants are preferred in the second, acid, containing component.

Examples of suitable anionic surfactants for use in the first component of the present invention include water soluble salts of the higher alkyl sulfates or sulfoacetate, such as sodium lauryl sulfate, sodium lauryl sulfoacetate or other suitable alkyl sulfates or sulfoacetates having 8 to 18 carbon atoms in the alkyl group; water soluble salts of sulfonated

monoglycerides of higher fatty acids, such as sodium coconut monoglyceride sulfonate or other suitable sulfonated monoglyceride of a fatty acid of 10 to 18 carbon atoms, sodium lauryl phosphate salts of amides of higher fatty acid, e g , 12 to 16 carbon atom acids, with lower aliphatic amino acids, e g., taurine or sarcosine, or other amino acid of 2 to 6 carbon atoms, such as sodium-N-methyl-N-palmitoyl tauride, sodium N-lauroyl-, N-myristoyl- and N-palmitoyl sarcosinates, water soluble salts of the esters of such fatty acids with isethionic acid or with glycerol monosulfate, such as the sodium salt of monosulfated monoglyceride of hydrogenated coconut oil fatty acids, water soluble salts of olefin sulfonates, e g., alkene sulfonates or hydroxyalkene sulfonates or mixtures thereof having 12 to 16 carbon atoms in the carbon chain of the molecule, and water soluble soaps of higher fatty acids, such as those of 12 to 18 carbon atoms, e g., coconut fatty acids

Examples of suitable nonionic surfactants for use in the second component of the present invention include condensates of sorbitan esters of fatty acids with ethylene oxide (polysorbates) such as sorbitan mono-oleate with from about 20 to about 60 moles of ethylene oxide A particularly preferred polysorbate is Polysorbate 20, polyoxyethylene 20 sorbitan monolaurate, marketed by ICI, Newcastle, Delaware 19720

Additional suitable nonionic surfactants useful in the second component of the present invention are the condensation products of an alpha-olefin oxide containing 10 to 20 carbon atoms, a polyhydric alcohol containing 2 to 10 carbon atoms and 2 to 6 hydroxyl groups, and either ethylene oxide or a mixture of ethylene oxide and propylene oxide The resultant surfactants are polymers which have a molecular weight in the range from about 400 to about 1600, contain from about 40% to about 80% ethylene oxide, by weight, and have an alpha-olefin oxide to polyhydric alcohol mole ratio in the range from about 1 1 to about 1 3, respectively Other nonionic surfactants useful in the present invention include condensates of sorbitan esters of fatty acids with polyethylene glycol such as sorbitan disostearate condensed with polyethylene glycol

The surface active agent can be present in one or both components of the compositions of the present invention, at a concentration of about 0.1 to about 5.0% by weight, preferably about 0.2 to about 1.5% by weight of the particular component.

Siliceous abrasive materials useful in the practice of the invention include, preferred silicas which have a mean particle size up to about 20 microns; including a precipitated amorphous hydrated silica, such as Zeodent 115, marketed by J.M. Huber Chemicals Division, Havre de Grace, Maryland 21078, or Sylodent 783 marketed by Grace Davidson, Baltimore, Maryland 21203.

The silica abrasive is present in each of the two dentifrice components of the present invention at a concentration from about 5 to about 30% by weight, and preferably about 5 to about 20% by weight of the respective component.

Fluoride Source Containing Component

The first component of the dentifrice composition of the present invention contains sodium fluoride, as the source of fluoride ions. The sodium fluoride is incorporated in the first component at a concentration of about 0.1 to about 3.0% by weight, and preferably at about 2.0 to about 2.5% by weight. At these preferred concentrations, about 4,500 ppm to over 5,600 ppm, fluoride ion will be available in solution, when the combined first and second components of the dentifrice composition are admixed and applied to the teeth.

It is also critical to the practice of the present invention that the first component be maintained at a pH of at least about 7.5, and preferably at a pH of at least about 8.0. Applicants' have discovered that NaF is stable in the presence of the siliceous abrasive only in a neutral or basic pH

environment. A buffering agent, such as sodium hydroxide and sodium bicarbonate or sodium phosphate may be employed to adjust the pH of the fluoride ion containing dentifrice component to the desired basic levels, if necessary

Acid Containing Component

The second component of the dentifrice composition of the present invention, which is maintained physically separate from the first component until mixing before use, contains an acid or mixture of acids, to acidulate the dentifrice when the two components are mixed prior to use Acidic compounds which can be present in the second component include both mineral and organic acids, such as, sulfuric acid, hydrochloric acid, malic acid, alginic acid, citric acid, succinic acid, lactic acid, tartaric acid, potassium bitartrate, acid sodium citrate, phosphoric acid, and sodium acid phosphate Acid phosphates are preferred, including phosphoric acid, or salts of phosphoric acid containing the radical PO_4, as such acids or acid salts thereof, such as sodium phosphate monobasic, not only provide the necessary acidity, but, also provide phosphate ions, to inhibit any tooth enamel demineralization which may occur with the application of the two component acidulated dentifrice to the teeth Further, the combination of an acid such as phosphoric acid and an acid salt, such as sodium phosphate monobasic, provides enhanced buffering to achieve the desired pH upon the mixing of the dentifrice components The preferred acid, phosphoric acid is commercially available as a liquid at 85% concentration and the preferred sodium phosphate monobasic is commercially available as a monohydrate powder

The acid is incorporated in the second component of the dentifrice composition of the present invention in a total concentration of about 0 7% to about 4% by weight and preferably at about 2 0 to about 3 0% by weight, the amount being sufficient to obtain a pH of from about 2 5 to about 5 0 and preferably from about 3 5 to about 4 5

The concentration of phosphate ions within the second component of the present invention is at least about 0.05 M, with a concentration of at least about 0.2 M preferred.

Other Ingredients Common to Both Components

Inorganic or organic thickeners may be included in the both of the components of the dentifrice of the present invention. Organic thickeners such as, natural and synthetic gums and colloids may also be incorporated in the present invention. Examples of such organic thickeners include carrageenan (Irish moss), xanthan gum and sodium carboxymethyl cellulose, starch, polyvinylpyrrolidone, hydroxyethylpropyl cellulose, hydroxybutyl methyl cellulose, hydroxypropylmethyl cellulose, and hydroxyethyl cellulose. Inorganic thickeners include amorphous silica compounds which function as thickening agents, such as colloidal silicas compounds available under tradenames such as Cab-o-sil fumed silica manufactured by Cabot Corporation and distributed by Lenape Chemical, Bound Brook, New Jersey, Zeodent 165 from J.M. Huber Chemicals Division, Havre de Grace, Maryland 21078, and Sylox 15 from Grace Davidson, Baltimore, Maryland 21203. A combination of inorganic and organic thickening agents are preferred and may be present in both components of the instant dentifrice in proportions of about 0.5 to about 15% by weight, preferably about 0.8 to about 6% in each of the two dentifrice components.

A striped dentifrice product may be obtained using the multicomponent dentifrice of the present invention, wherein colorants of contrasting colors are incorporated in each of the dentifrice components to be dispensed; the colorants being non-toxic when used in the suggested amounts. Colorants used in the practice of the present invention include both pigments and dyes.

Pigments used in the practice of the present invention include non-toxic, water insoluble inorganic pigments such as titanium dioxide (TiO_2)

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and chromium oxide greens, ultramarine blues and pinks and ferric oxides Dyes include water insoluble dye lakes prepared by extending calcium or aluminum salts of FD&C dyes on alumina such as FD&C Green #1 lake, FD&C Blue #2 lake, FD&C R&D #30 lake and FD&C # Yellow 15 lake The concentration of the pigment or dye in the dentifrice composition ranges in amount from about 0 0005 percent to about 2 percent by weight of the respective component.

Other ingredients which may be incorporated in one or both components of the present invention, include antibacterial agents, antitartar actives, sweetener, flavor and preservatives, such as sodium benzoate

Preferred antibacterial agents are non-cationic antibacterial agents based on phenolic and bisphenolic compounds, halogenated diphenyl ethers such as triclosan, benzoate esters and carbanilides Cationic antibacterial agents which are also preferred, including quaternary ammonium salts, such as, chlorhexidine digluconate, can only be included in the second acid containing component of the present invention Such antibacterial agents can be present in quantities of from about 0 03 to about 1% by weight of the particular component.

Antitartar actives such as sodium tripolyphosphate, tetrapotassium or tetrasodium pyrophosphates, or mixtures thereof, can be present in concentrations from about 0 5 to about 8% by weight of the particular component in which such actives are stable The sweetener content will normally be that of an artificial or synthetic sweetener and the normal proportion thereof present will be in the range of 0 1 to 1% by weight of the respective component, preferably 0 2 to 0 5% by weight the respective component The flavor content, which is preferably a fruit or mixed peppermint/menthol flavor, will usually be in the range of 0 5 to 2% by weight of the respective component, preferably 0 5 to 1 0% by weight of the respective component. The contents of other components or adjuvants will

normally not exceed 10% by weight, often will be less than 5% by weight, and can be as low as 0%.

When noncationic antibacterial agents are included in any of the dentifrice components, there is also preferably included from about 0.05 to about 5% of an antibacterial enhancing agent (AEA) which enhances the delivery and retention of the noncationic antibacterial agent to, and retention thereof on oral surfaces. AEA's useful in the present invention are disclosed in U.S. Patents 5,188,821 and 5,192,531; and include synthetic anionic polymeric polycarboxylates, in the form 1:4 to 4:1 copolymers of maleic anhydride or acid with another polymerizable ethylenically unsaturated monomer, preferably methyl vinyl ether/maleic anhydride having a molecular weight (M.W.) of about 30,000 to about 1,000,000, most preferably about 30,000 to about 800,000. These copolymers are available for example as Gantrez, e.g. AN 139 (M.W. 500,000), AN 119 (M.W. 250,000) and preferably S-97 Pharmaceutical Grade (M.W. 700,000) available from ISP Technologies, Inc., Bound Brook, N.J. 08805.

Preparation of the Dentifrice

To prepare either of the dentifrice components of the present invention, generally the humectants e.g. glycerin, propylene glycol, polyethylene glycol ingredients, are dispersed with any sweetener and water in a conventional mixer, until the mixture becomes a homogeneous gel phase. Into the gel phase are added a pigment such as TiO_2, any antibacterial agent such as triclosan, any antibacterial enhancing agent such as Gantrez, any tartar control agents such as tetrasodium pyrophosphate or sodium tripolyphosphate or both, in the second component the acid phosphate, and in the first component the fluoride ion source, i.e. sodium fluoride. These ingredients are mixed until a homogenous phase is obtained. Thereafter the thickener, silica abrasive, flavor and surfactant ingredients are added and the ingredients mixed at high speed under vacuum of from about 20 to 100 mm of Hg. The resultant

product is in the case of each component is a homogeneous, semi-solid, extrudable paste product

Packaging of the Dentifrice

The multicomponent dentifrice composition of the present invention is packaged in a suitable dispensing container in which the components are maintained physically separated and from which the separated components may be dispensed synchronously as a ribbon for application to a toothbrush Such containers are known in the art. An example of such a container is a two compartment dispensing container, such as a pump or tube, having collapsible sidewalls, as disclosed in U S Patents 4,487,757 and 4,687,663, wherein, the container body is formed from a collapsible plastic web and is provided with a partition within the container body defining separate compartments in which the physically separated components are stored and from which they are dispensed through a suitable dispensing outlet

The following example is further illustrative the present invention, but it is understood that the invention is not limited thereto All amounts and proportions referred to herein and in the appended claims are by weight, unless otherwise stated

EXAMPLE

A two component dentifrice of the present invention was prepared, designated Toothpaste I, having a first sodium fluoride and silica abrasive containing component and a second acid phosphate and silica abrasive containing component The ingredients and pH of each of the two components of Toothpaste I are itemized in Table I, below

Table I

Toothpaste I

Ingredients	1st Component (in weight %)	2nd Component (in weight %)
PEG 600	3.00	3.00
Xanthan Gum	0.80	0.80
Sorbitol	37.15	36.58
Water	39.24	38.24
Sodium fluoride*	2.21	-----
Sodium benzoate	0.50	0.50
Phosphoric Acid 85%	----	0.96
Sodium phosphate monobasic	-----	1.82
Sodium saccharin	0.25	0.25
Dye	0.50	0.50
Sylox 15	10.0	10.0
Zeodent 115	5.35	5.35
Polysorbate 20	-----	0.50
Sodium Lauryl Sulfate	1.0	----
Flavor	0.50	0.50
Total %	100%	100%
pH	8.0	3.5

*Contains potentially 5000 ppm releasable F^- with combination of 1st and 2nd components upon admixing prior to application to the dentiture.

To determine the fluoride ion availability of the multicomponent dentifrice of the present invention, after storage for a period of 8 weeks, the 1st and 2nd components of Toothpaste I were mixed together, diluted one-thousand times using a commercially available buffering solution (Orion TISAB II), at ambient room temperature; the available fluoride ion concentration was determined using a Corning Model 350 pH/ion Analyzer, Corning Inc., Corning N.Y, equipped with a Orion Fluoride Electrode, Model #94-09, Orion Research Products, Boston, Mass. The EMF output from the

Orion Fluoride Electrode was converted to ppm fluoride by means of a logarithmic-linear calibration established with known concentrations of fluoride in the buffering solution and the resultant ppm of available fluoride determined has been recorded in Table III, below

For purposes of comparison, the procedure was repeated except the dentifrice assayed for fluoride availability was a single component acidulated phosphate fluoride dentifrice of the prior art, containing a silica abrasive designated,

Toothpaste II, having the ingredients and pH listed in Table II, below Referring to Table II, note that the amount of sodium fluoride within Toothpaste II is one-half that of the 1st Component of Toothpaste I, so that a comparable potential 5,000 ppm of fluoride would be delivered upon use by each. After a comparable eight weeks of storage, the available soluble fluoride of Toothpaste II was assayed using the same methodology as that used for Toothpaste I and the results are also recorded in Table III, below

Table II

Toothpaste II

Ingredients	Composition (in weight %)
PEG 600	3.00
Xanthan Gum	0.80
Sorbitol	34.37
Water	39.345
Sodium fluoride	1.105
Sodium benzoate	0.50
Phosphoric Acid 85%	0.96
Sodium phosphate monobasic	1.82
Sodium saccharin	0.25
Dye	0.50
Sylox 15	10.0
Zeodent 115	5.35
Polysorbate 20	0.50
Sodium Lauryl Sulfate	1.0
Flavor	0.50
Total %	100%
pH	5.0

Table III

Fluoride Availability

Toothpaste Analyzed	Available Soluble Fluoride Ion (in ppm)
Toothpaste I	4,900
Toothpaste II	3,800

Referring to Table III, the 4,900 ppm is equivalent to 98% availability of the fluoride in Toothpaste I and the 3,800 ppm is correspondingly equivalent to 76% fluoride availability in Toothpaste II The 22% difference in available fluoride between Toothpaste I of the present invention and comparative Toothpaste II is significant and unexpectedly large The magnitude of the loss of available fluoride in Toothpaste II is at a level of significance rendering Toothpaste II commercially unacceptable

What is claimed is:

1. A method for the fluoridation of teeth utilizing a two component dentifrice system which is free of any water soluble calcium salts comprising the steps of (1) preparing a first dentifrice component containing from about 2.0% to about 2.5% by weight sodium fluoride as the fluoridation source and having a pH of at least about 7.5, and a second fluoride free, dentifrice component containing a source of phosphate ions and an acid in an amount sufficient to maintain the pH in the range of about 2.5 to about 5.0; both dentifrice components containing a siliceous abrasive; (2) maintaining the first and second dentifrice components separate from the other until application to teeth requiring fluoridation; (3) mixing the first and second components together to form a mixture having a pH of from about 4.0 to about 6.0, (4) applying the mixture to the teeth, whereby enhanced availability of fluoride ions to tooth enamel is observed.

2. The method of claim 1, wherein the source of phosphate ions is phosphoric acid, sodium phosphate monobasic or a combination thereof.

3. The method of claim 1, wherein the first component contains from about 0.1 to about 3.0% by weight sodium fluoride.

4. The method of claim 1, wherein the second component contains from about 0.7 to about 4% by weight of an acid phosphate and an acid salt.

5. The method of claim 4, wherein the acid phosphate is phosphoric acid and the acid salt is sodium phosphate monobasic.

6. The method of claim 1, wherein the pH of the first component is at least about pH 8.0.

7 The method of claim 1, wherein the acid is in an amount sufficient to maintain the pH of the second component in the range of about pH 3 5 to about pH 4 5

8 The method of claim 1, wherein the siliceous abrasive is a precipitated amorphous hydrated silica.

9 The method of claim 8, wherein the dentifrice composition contains from 10 to 30% in total of the amorphous hydrated silica abrasive

10 The method of claim 9, wherein both components of the dentifrice system each contain 15 35% by weight of the amorphous hydrated silica abrasive

11 The method of claim 1, wherein a surfactant is incorporated in both components of the dentifrice system

12. The method of claim 11, wherein the surfactant incorporated in the first component of the dentifrice system is sodium lauryl sulfate and the surfactant incorporated in the second component of the dentifrice is a condensate of sorbitan esters of fatty acids with ethylene oxide

PCT REQUEST 6088-01

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0	For receiving Office use only	
0-1	International Application No.	
0-2	International Filing Date	
0-3	Name of receiving Office and "PCT International Application"	

0-4	Form - PCT/RO/101 PCT Request	
0-4-1	Prepared using	PCT-EASY Version 2.91 (updated 01.01.2001)
0-5	Petition The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty	
0-6	Receiving Office (specified by the applicant)	United States Patent and Trademark Office (USPTO) (RO/US)
0-7	Applicant's or agent's file reference	6088-01
I	Title of invention	DUAL COMPONENT DENTIFRICE COMPOSITION FOR FLUORIDATING TEETH
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V	Designation of States	
V-1	Regional Patent (other kinds of protection or treatment, if any are specified between parentheses after the designation(s) concerned)	AP GH GM KE LS MW MZ SD SL SZ TZ UG ZW and any other State which is a Contracting State of the Harare Protocol and of the PCT EA AM AZ BY KG KZ MD RU TJ TM and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT EP AT BE CH&LI CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR and any other State which is a Contracting State of the European Patent Convention and of the PCT OA BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG and any other State which is a member State of OAPI and a Contracting State of the PCT

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V-2	National Patent (other kinds of protection or treatment, if any are specified between parentheses after the designation(s) concerned)	AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH&LI CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ ~~VN YU ZA~~ ZW	
V-3	National Patent (States which have become party to the PCT after the issuance of this version of EASY)	CO Colombia	
V-5	Precautionary Designation Statement In addition to the designations made under items V-1 V-2 and V-3 the applicant also makes under Rule 4 9(b) all designations which would be permitted under the PCT except any designation(s) of the State(s) indicated under item V-5 below The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit.		
V-6	Exclusion(s) from precautionary designations	NONE	
VI 1	Priority claim of earlier national application		
VI-1-1	Filing date	06 March 2000 (06 03 2000)	
VI 1-2	Number	09/519,507	
VI-1-3	Country	US	
VI-2	Priority document request The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) identified above as item(s)	VI-1	
VII 1	International Searching Authority Chosen	European Patent Office (EPO) (ISA/EP)	
VIII	Check list	number of sheets	electronic file(s) attached
VIII 1	Request	4	-
VIII-2	Description	15	-
VIII-3	Claims	2	-
VIII-4	Abstract	1	EZABST00 TXT
VIII-5	Drawings	0	-
VIII-7	TOTAL	22	
	Accompanying Items	paper document(s) attached	electronic file(s) attached
VIII-8	Fee calculation sheet	✓	-
VIII-16	PCT EASY diskette	-	diskette
VIII-17	Figure of the drawings which should accompany the abstract		
VIII-19	Language of filing of the international application	English	

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IX-1	Signature of applicant or agent	Paul Shapiro
IX-1-1	Name (LAST First)	SHAPIRO, Paul

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10-1	Date of actual receipt of the purported international application	
10-2	Drawings	
10-2-1	Received	
10-2-2	Not received	
10-3	Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application	
10-4	Date of timely receipt of the required corrections under PCT Article 11(2)	
10-5	International Searching Authority	ISA/EP
10-6	Transmittal of search copy delayed until search fee is paid	

FOR INTERNATIONAL BUREAU USE ONLY

11-1	Date of receipt of the record copy by the International Bureau	

39

DUAL COMPONENT DENTIFRICE COMPOSITION FOR FLUORIDATING TEETH

Background Of The Invention

1 Field of the Invention

This invention is directed to a dentifrice composition containing acidulated fluoride compounds effective as anticaries agents and more particularly to an acidulated phosphate fluoride dual component dentifrice composition for fluoridating teeth

2 The Prior Art

It has long been known to include fluoride containing compounds in dentifrices as anticaries agents, and it has been established that these compounds are effective to reduce the incidence of dental caries Fluoride compounds which are deemed to be the most effective are sodium fluoride, sodium monoflurophosphate and stannous fluoride The fluoride compounds are effective mainly due to the fluoride ions which improve the acid resistance of tooth enamel and accelerate remineralization (i e recalcification) of decayed teeth in their early stage when the decalcification has proceeded only slightly The effect of improving the acid resistance of the enamel is believed to be due to the fact that the fluoride ions are incorporated into a crystal lattice of hydroxyapatite which is the main constituent of tooth enamel or, in other words, fluoride ions partially fluoridate hydroxyapatite and simultaneously repair the lattice irregularities

The effectiveness of fluoride treatment in providing acid resistance to tooth enamel is dependent upon the amount of fluoride ion which is

available for deposition on the enamel being treated Also, using phosphate buffered NaF, the incorporation of fluoride as CaF_2 into dental enamel is facilitated at lower pH levels which increase enamel solubility Prencipe et al , Colloid & Surface Chemistry, 4th Chemical Congress of America, NY (Aug 25-30, 1991) It is, therefore, desirable to formulate an acidulated phosphate fluoride dentifrice to enhance fluoride deposition onto and uptake into the tooth enamel.

Acidulated phosphate fluoride is disclosed in U S Patents 4,080,440 and 5,603,992 as delivered in a dual component dentifrice comprised of a separately housed first acidic component containing a fluoride salt such as NaF, which with a second separately housed cationic calcium ion containing component, forms the two component dentifrice for tooth remineralization While these two separately housed component formulations avoid any reactions between ingredients within the first and second components during storage, upon application to the teeth the fluoride salt will begin to react with the cationic calcium ion, reducing the availability of the fluoride for fluoridation of the teeth Further, a reaction occurs during storage within the first component itself, between the acid, the sodium fluoride and the silica abrasive therein, reducing the bioavailability of the fluoride ion The amorphous silica abrasive ingredient generally used in dentifrices is one of the most chemically inert abrasives available, however, the negatively charged oxygen atoms of the silica are protonated in the acid environment, and the resulting hydroxyl (OH) moieties hydrogen bond to the available fluoride ions released from the sodium fluoride This fluoride-OH bond occurs in the acidulated phosphate fluoride silica abrasive systems disclosed in prior art Patents 4,080,440, and 5603,922 whereby, the availability of the fluoride ions present in the dentifrice to fluoridate the enamel upon application thereto is significantly reduced The magnitude of this reduction in available fluoride is hereinafter demonstrated

Thus, there is a clear need to formulate a stable, acidulated phosphate fluoride dentifrice, having the maximum deliverable fluoride

SUMMARY OF THE INVENTION

In accordance with the present invention there is provided a method for the fluoridation of tooth enamel using a multicomponent dentifrice comprised of two separately housed, semi-solid aqueous components, the first component containing sodium fluoride as a source of fluoride ions, in an orally acceptable vehicle having a pH of at least about 7 5 and, the second component which is fluoride free containing both a source of phosphate ions and an acid to provide a pH of from about 2 5 to about 5 0, in an orally acceptable vehicle, each component containing a siliceous abrasive and each component being free of any cationic calcium ion containing component, such as water soluble calcium salts, whereby upon mixing of the components, a mixture having a pH of from about 4 0 to about 6 0 is formed, whereby upon application of the mixture to the teeth, the availability of fluoride ions is enhanced

There has been no recognition in the prior art of the significant loss of fluoride availability during extended periods of storage, resulting from the interaction of generally inert silica abrasives, with sodium fluoride, when NaF is present as the fluoride source in dentifrices having an acid environment In accordance with the present invention, as will be further demonstrated herein, the enhanced fluoride availability resulting from separating the acid and the fluoride in separate dentifrice components, each containing a silica abrasive, is unexpected and significant

Description Of The Preferred Embodiments

In use, the components of the two component dentifrice of the present invention comprise a first sodium fluoride and silica abrasive containing dentifrice component, and a second acid and silica abrasive containing dentifrice component, these two components are preferably combined in approximately equal weight proportions, so that about one-half of the concentration of any particular ingredient within either component

will be present when the components are combined and applied to the teeth, as by brushing Both components are formulated to provide similar apparent physical characteristics, so that the two components are simultaneously delivered in the desired predetermined amounts by extrusion from a multicompartmented tube or pump device

Dentifrice Vehicle Common to Both Components

In the preparation of the individual dentifrice components of the present invention, the respective sodium fluoride or acid is incorporated within a dentifrice vehicle suitable for use in the oral cavity, which contains water, humectant, surfactant and a polishing agent or abrasive The humectant is generally a mixture of humectants, such as glycerol, sorbitol and polyethylene glycol of a molecular weight in the range of 200-1000, but other mixtures of humectants and single humectants may also be employed The humectant content within each of the two components is in the range about of 20% to about 50% by weight and preferably about 30 to about 45% by weight The water content is from about 20% to about 45%, and preferably about 30 to about 42% by weight

Surface active agents or surfactants may be incorporated in the vehicle of the individual components of the present invention, as an ingredient to aid in the thorough dispersion of the dentifrice throughout the oral cavity when applied thereto, as well as, to improve the dentifrice's cosmetic acceptability and the foaming properties Anionic surfactants are preferred in the first, sodium fluoride, containing component Nonionic surfactants are preferred in the second, acid, containing component

Examples of suitable anionic surfactants for use in the first component of the present invention include water soluble salts of the higher alkyl sulfates or sulfoacetate, such as sodium lauryl sulfate, sodium lauryl sulfoacetate or other suitable alkyl sulfates or sulfoacetates having 8 to 18 carbon atoms in the alkyl group, water soluble salts of sulfonated

monoglycerides of higher fatty acids, such as sodium coconut monoglyceride sulfonate or other suitable sulfonated monoglyceride of a fatty acid of 10 to 18 carbon atoms, sodium lauryl phosphate salts of amides of higher fatty acid, e g , 12 to 16 carbon atom acids, with lower aliphatic amino acids, e g , taurine or sarcosine, or other amino acid of 2 to 6 carbon atoms, such as sodium-N-methyl-N-palmitoyl tauride, sodium N-lauroyl-, N-myristoyl- and N-palmitoyl sarcosinates, water soluble salts of the esters of such fatty acids with isethionic acid or with glycerol monosulfate, such as the sodium salt of monosulfated monoglyceride of hydrogenated coconut oil fatty acids, water soluble salts of olefin sulfonates, e g , alkene sulfonates or hydroxyalkene sulfonates or mixtures thereof having 12 to 16 carbon atoms in the carbon chain of the molecule, and water soluble soaps of higher fatty acids, such as those of 12 to 18 carbon atoms, e g , coconut fatty acids

Examples of suitable nonionic surfactants for use in the second component of the present invention include condensates of sorbitan esters of fatty acids with ethylene oxide (polysorbates) such as sorbitan mono-oleate with from about 20 to about 60 moles of ethylene oxide A particularly preferred polysorbate is Polysorbate 20, polyoxyethylene 20 sorbitan monolaurate, marketed by ICI, Newcastle, Delaware 19720

Additional suitable nonionic surfactants useful in the second component of the present invention are the condensation products of an alpha-olefin oxide containing 10 to 20 carbon atoms, a polyhydric alcohol containing 2 to 10 carbon atoms and 2 to 6 hydroxyl groups, and either ethylene oxide or a mixture of ethylene oxide and propylene oxide The resultant surfactants are polymers which have a molecular weight in the range from about 400 to about 1600, contain from about 40% to about 80% ethylene oxide, by weight, and have an alpha-olefin oxide to polyhydric alcohol mole ratio in the range from about 1 1 to about 1 3, respectively Other nonionic surfactants useful in the present invention include condensates of sorbitan esters of fatty acids with polyethylene glycol such as sorbitan diisostearate condensed with polyethylene glycol

The surface active agent can be present in one or both components of the compositions of the present invention, at a concentration of about 0 1 to about 5 0% by weight, preferably about 0 2 to about 1 5% by weight of the particular component

Siliceous abrasive materials useful in the practice of the invention include, preferred silicas which have a mean particle size up to about 20 microns, including a precipitated amorphous hydrated silica, such as Zeodent 115, marketed by J M Huber Chemicals Division, Havre de Grace, Maryland 21078, or Sylodent 783 marketed by Grace Davidson, Baltimore, Maryland 21203

The silica abrasive is present in each of the two dentifrice components of the present invention at a concentration from about 5 to about 30% by weight, and preferably about 5 to about 20% by weight of the respective component

Fluoride Source Containing Component

The first component of the dentifrice composition of the present invention contains sodium fluoride, as the source of fluoride ions The sodium fluoride is incorporated in the first component at a concentration of about 0 1 to about 3 0% by weight, and preferably at about 2 0 to about 2 5% by weight At these preferred concentrations, about 4,500 ppm to over 5,600 ppm, fluoride ion will be available in solution, when the combined first and second components of the dentifrice composition are admixed and applied to the teeth

It is also critical to the practice of the present invention that the first component be maintained at a pH of at least about 7 5, and preferably at a pH of at least about 8 0 Applicants' have discovered that NaF is stable in the presence of the siliceous abrasive only in a neutral or basic pH

environment A buffering agent, such as sodium hydroxide and sodium bicarbonate or sodium phosphate may be employed to adjust the pH of the fluoride ion containing dentifrice component to the desired basic levels, if necessary

Acid Containing Component

The second component of the dentifrice composition of the present invention, which is maintained physically separate from the first component until mixing before use, contains an acid or mixture of acids, to acidulate the dentifrice when the two components are mixed prior to use Acidic compounds which can be present in the second component include both mineral and organic acids, such as, sulfuric acid, hydrochloric acid, malic acid, alginic acid, citric acid, succinic acid, lactic acid, tartaric acid, potassium bitartrate, acid sodium citrate, phosphoric acid, and sodium acid phosphate Acid phosphates are preferred, including phosphoric acid, or salts of phosphoric acid containing the radical PO_4, as such acids or acid salts thereof, such as sodium phosphate monobasic, not only provide the necessary acidity, but, also provide phosphate ions, to inhibit any tooth enamel demineralization which may occur with the application of the two component acidulated dentifrice to the teeth Further, the combination of an acid such as phosphoric acid and an acid salt, such as sodium phosphate monobasic, provides enhanced buffering to achieve the desired pH upon the mixing of the dentifrice components The preferred acid, phosphoric acid is commercially available as a liquid at 85% concentration and the preferred sodium phosphate monobasic is commercially available as a monohydrate powder

The acid is incorporated in the second component of the dentifrice composition of the present invention in a total concentration of about 0 7% to about 4% by weight and preferably at about 2 0 to about 3 0% by weight, the amount being sufficient to obtain a pH of from about 2 5 to about 5 0 and preferably from about 3 5 to about 4 5

The concentration of phosphate ions within the second component of the present invention is at least about 0 05 M, with a concentration of at least about 0 2 M preferred

Other Ingredients Common to Both Components

Inorganic or organic thickeners may be included in the both of the components of the dentifrice of the present invention Organic thickeners such as, natural and synthetic gums and colloids may also be incorporated in the present invention Examples of such organic thickeners include carrageenan (Irish moss), xanthan gum and sodium carboxymethyl cellulose, starch, polyvinylpyrrolidone, hydroxyethylpropyl cellulose, hydroxybutyl methyl cellulose, hydroxypropylmethyl cellulose, and hydroxyethyl cellulose Inorganic thickeners include amorphous silica compounds which function as thickening agents, such as colloidal silicas compounds available under tradenames such as Cab-o-sil fumed silica manufactured by Cabot Corporation and distributed by Lenape Chemical, Bound Brook, New Jersey, Zeodent 165 from J M Huber Chemicals Division, Havre de Grace, Maryland 21078, and Sylox 15 from Grace Davidson, Baltimore, Maryland 21203 A combination of inorganic and organic thickening agents are preferred and may be present in both components of the instant dentifrice in proportions of about 0 5 to about 15% by weight, preferably about 0 8 to about 6% in each of the two dentifrice components

A striped dentifrice product may be obtained using the multicomponent dentifrice of the present invention, wherein colorants of contrasting colors are incorporated in each of the dentifrice components to be dispensed, the colorants being non-toxic when used in the suggested amounts Colorants used in the practice of the present invention include both pigments and dyes

Pigments used in the practice of the present invention include non-toxic, water insoluble inorganic pigments such as titanium dioxide (TiO_2)

and chromium oxide greens, ultramarine blues and pinks and ferric oxides Dyes include water insoluble dye lakes prepared by extending calcium or aluminum salts of FD&C dyes on alumina such as FD&C Green #1 lake, FD&C Blue #2 lake, FD&C R&D #30 lake and FD&C # Yellow 15 lake The concentration of the pigment or dye in the dentifrice composition ranges in amount from about 0 0005 percent to about 2 percent by weight of the respective component

Other ingredients which may be incorporated in one or both components of the present invention, include antibacterial agents, antitartar actives, sweetener, flavor and preservatives, such as sodium benzoate

Preferred antibacterial agents are non-cationic antibacterial agents based on phenolic and bisphenolic compounds, halogenated diphenyl ethers such as triclosan, benzoate esters and carbanilides Cationic antibacterial agents which are also preferred, including quaternary ammonium salts, such as, chlorhexidine digluconate, can only be included in the second acid containing component of the present invention Such antibacterial agents can be present in quantities of from about 0 03 to about 1% by weight of the particular component

Antitartar actives such as sodium tripolyphosphate, tetrapotassium or tetrasodium pyrophosphates, or mixtures thereof, can be present in concentrations from about 0 5 to about 8% by weight of the particular component in which such actives are stable The sweetener content will normally be that of an artificial or synthetic sweetener and the normal proportion thereof present will be in the range of 0 1 to 1% by weight of the respective component, preferably 0 2 to 0 5% by weight the respective component The flavor content, which is preferably a fruit or mixed peppermint/menthol flavor, will usually be in the range of 0 5 to 2% by weight of the respective component, preferably 0 5 to 1 0% by weight of the respective component The contents of other components or adjuvants will

normally not exceed 10% by weight, often will be less than 5% by weight, and can be as low as 0%

When noncationic antibacterial agents are included in any of the dentifrice components, there is also preferably included from about 0 05 to about 5% of an antibacterial enhancing agent (AEA) which enhances the delivery and retention of the noncationic antibacterial agent to, and retention thereof on oral surfaces AEA's useful in the present invention are disclosed in U S Patents 5,188,821 and 5,192,531, and include synthetic anionic polymeric polycarboxylates, in the form 1 4 to 4 1 copolymers of maleic anhydride or acid with another polymerizable ethylenically unsaturated monomer, preferably methyl vinyl ether/maleic anhydride having a molecular weight (M W) of about 30,000 to about 1,000,000, most preferably about 30,000 to about 800,000 These copolymers are available for example as Gantrez, e g AN 139 (M W 500,000), AN 119 (M W 250,000) and preferably S-97 Pharmaceutical Grade (M W 700,000) available from ISP Technologies, Inc , Bound Brook, N J 08805

Preparation of the Dentifrice

To prepare either of the dentifrice components of the present invention, generally the humectants e g glycerin, propylene glycol, polyethylene glycol ingredients, are dispersed with any sweetener and water in a conventional mixer, until the mixture becomes a homogeneous gel phase Into the gel phase are added a pigment such as TiO_2, any antibacterial agent such as triclosan, any antibacterial enhancing agent such as Gantrez, any tartar control agents such as tetrasodium pyrophosphate or sodium tripolyphosphate or both, in the second component the acid phosphate, and in the first component the fluoride ion source, i e sodium fluoride These ingredients are mixed until a homogenous phase is obtained Thereafter the thickener, silica abrasive, flavor and surfactant ingredients are added and the ingredients mixed at high speed under vacuum of from about 20 to 100 mm of Hg The resultant

product is in the case of each component is a homogeneous, semi-solid, extrudable paste product

Packaging of the Dentifrice

The multicomponent dentifrice composition of the present invention is packaged in a suitable dispensing container in which the components are maintained physically separated and from which the separated components may be dispensed synchronously as a ribbon for application to a toothbrush Such containers are known in the art An example of such a container is a two compartment dispensing container, such as a pump or tube, having collapsible sidewalls, as disclosed in U S Patents 4,487,757 and 4,687,663, wherein, the container body is formed from a collapsible plastic web and is provided with a partition within the container body defining separate compartments in which the physically separated components are stored and from which they are dispensed through a suitable dispensing outlet

The following example is further illustrative the present invention, but it is understood that the invention is not limited thereto All amounts and proportions referred to herein and in the appended claims are by weight, unless otherwise stated

EXAMPLE

A two component dentifrice of the present invention was prepared, designated Toothpaste I, having a first sodium fluoride and silica abrasive containing component and a second acid phosphate and silica abrasive containing component The ingredients and pH of each of the two components of Toothpaste I are itemized in Table I, below

Table I

Toothpaste I

Ingredients	1st Component (in weight %)	2nd Component (in weight %)
PEG 600	3 00	3,00
Xanthan Gum	0 80	0 80
Sorbitol	37 15	36 58
Water	39 24	38 24
Sodium fluoride*	2 21	-----
Sodium benzoate	0 50	0 50
Phosphonic Acid 85%	-----	0 96
Sodium phosphate monobasic	-----	1 82
Sodium saccharin	0 25	0 25
Dye	0 50	0 50
Sylox 15	10 0	10 0
Zeodent 115	5 35	5 35
Polysorbate 20	-----	0 50
Sodium Lauryl Sulfate	1 0	-----
Flavor	0 50	0 50
Total %	100%	100%
pH	8 0	3 5

*Contains potentially 5000 ppm releasable F^- with combination of 1st and 2nd components upon admixing prior to application to the denture

To determine the fluoride ion availability of the multicomponent dentifrice of the present invention, after storage for a period of 8 weeks, the 1st and 2nd components of Toothpaste I were mixed together, diluted one-thousand times using a commercially available buffering solution (Orion TISAB II), at ambient room temperature, the available fluoride ion concentration was determined using a Corning Model 350 pH/ion Analyzer, Corning Inc , Corning N Y, equipped with a Orion Fluoride Electrode, Model #94-09, Orion Research Products, Boston, Mass The EMF output from the

Orion Fluoride Electrode was converted to ppm fluoride by means of a logarithmic-linear calibration established with known concentrations of fluoride in the buffering solution and the resultant ppm of available fluoride determined has been recorded in Table III, below

For purposes of comparison, the procedure was repeated except the dentifrice assayed for fluoride availability was a single component acidulated phosphate fluoride dentifrice of the prior art, containing a silica abrasive designated,

Toothpaste II, having the ingredients and pH listed in Table II, below Referring to Table II, note that the amount of sodium fluoride within Toothpaste II is one-half that of the 1st Component of Toothpaste I, so that a comparable potential 5,000 ppm of fluoride would be delivered upon use by each After a comparable eight weeks of storage, the available soluble fluoride of Toothpaste II was assayed using the same methodology as that used for Toothpaste I and the results are also recorded in Table III, below

Table II

Toothpaste II

Ingredients	Composition (in weight %)
PEG 600	3 00
Xanthan Gum	0 80
Sorbitol	34 37
Water	39 345
Sodium fluoride	1 105
Sodium benzoate	0 50
Phosphoric Acid 85%	0 96
Sodium phosphate monobasic	1 82
Sodium saccharin	0 25
Dye	0 50
Sylox 15	10 0
Zeodent 115	5 35
Polysorbate 20	0 50
Sodium Lauryl Sulfate	1 0
Flavor	0 50
Total %	100%
pH	5 0

Table III

Fluoride Availability

Toothpaste Analyzed	Available Soluble Fluoride Ion (in ppm)
Toothpaste I	4,900
Toothpaste II	3,800

Referring to Table III, the 4,900 ppm is equivalent to 98% availability of the fluoride in Toothpaste I and the 3,800 ppm is correspondingly equivalent to 76% fluoride availability in Toothpaste II. The 22% difference in available fluoride between Toothpaste I of the present invention and comparative Toothpaste II is significant and unexpectedly large The magnitude of the loss of available fluoride in Toothpaste II is at a level of significance rendering Toothpaste II commercially unacceptable

What is claimed is

1 A method for the fluoridation of teeth utilizing a two component dentifrice system which is free of any water soluble calcium salts comprising the steps of (1) preparing a first dentifrice component containing from about 2 0% to about 2 5% by weight sodium fluoride as the fluoridation source and having a pH of at least about 7 5, and a second fluoride free, dentifrice component containing a source of phosphate ions and an acid in an amount sufficient to maintain the pH in the range of about 2 5 to about 5 0, both dentifrice components containing a siliceous abrasive, (2) maintaining the first and second dentifrice components separate from the other until application to teeth requiring fluoridation, (3) mixing the first and second components together to form a mixture having a pH of from about 4 0 to about 6 0, (4) applying the mixture to the teeth, whereby enhanced availability of fluoride ions to tooth enamel is observed

2 The method of claim 1, wherein the source of phosphate ions is phosphoric acid, sodium phosphate monobasic or a combination thereof

3 The method of claim 1, wherein the first component contains from about 0 1 to about 3 0% by weight sodium fluoride

4 The method of claim 1, wherein the second component contains from about 0 7 to about 4% by weight of an acid phosphate and an acid salt

5 The method of claim 4, wherein the acid phosphate is phosphoric acid and the acid salt is sodium phosphate monobasic

6 The method of claim 1, wherein the pH of the first component is at least about pH 8 0

7 The method of claim 1, wherein the acid is in an amount sufficient to maintain the pH of the second component in the range of about pH 3 5 to about pH 4 5

8 The method of claim 1, wherein the siliceous abrasive is a precipitated amorphous hydrated silica.

9 The method of claim 8, wherein the dentifrice composition contains from 10 to 30% in total of the amorphous hydrated silica abrasive

10 The method of claim 9, wherein both components of the dentifrice system each contain 15 35% by weight of the amorphous hydrated silica abrasive

11 The method of claim 1, wherein a surfactant is incorporated in both components of the dentifrice system

12 The method of claim 11, wherein the surfactant incorporated in the first component of the dentifrice system is sodium lauryl sulfate and the surfactant incorporated in the second component of the dentifrice is a condensate of sorbitan esters of fatty acids with ethylene oxide

ABSTRACT

A method is disclosed for enhancing fluoride availability using an acidulated two component dentifrice system in which the first component contains sodium fluoride and a silica abrasive in an alkaline environment and the second component contains an acid, a phosphate ion source, and a silica abrasive

PCT

GENERAL POWER OF ATTORNEY

(for several international applications filed under the Patent Cooperation Treaty)

(PCT Rule 90 5)

The undersigned person(s)
(Family name followed by given name, for a full legal entity full official designation. The address must include postal code and name of country.)

COLGATE-PALMOLIVE COMPANY
300 Park Avenue
New York New York 10022
United States of America

hereby appoint(s) the following person as ☒ agent ☐ common representative

Name and address
(Family name followed by given name for a legal entity, full official designation. The address must include postal code and name of country.)

Martin B Barancik Henry S Goldfine Bernard Lieberman Michael J McGreal Rosemary M Miano, Richard E Nanfeldt and Paul Shapiro of

COLGATE-PALMOLIVE COMPANY
909 River Road
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Piscataway New Jersey 08855-1343
United States of America

to represent the undersigned before

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Signature(s) *(where there are several persons each of them must sign, next to each signature indicate the name of the person signing and the capacity in which the person signs if such capacity is not obvious from reading this power)*

Paul Shapiro
Vice President
Chief Patent Counsel

Date November 1 2000

PCT (ANNEX - FEE CALCULATION SHEET)

6088-01

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0	For receiving Office use only	
0-1	International Application No	
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0-4	Form PCT/RO/101 (Annex) PCT Fee Calculation Sheet				
0-4-1	Prepared using		PCT-EASY Version 2 91 (updated 01 01 2001)		
0-9	Applicant's or agent's file reference		6088-01		
2	Applicant		COLGATE-PALMOLIVE COMPANY		
12	Calculation of prescribed fees		fee amount/multiplier	total amounts (USD)	
12 1	Transmittal fee	T	⇨	240	
12-2	Search fee	S	⇨	846	
12-3	International fee				
	Basic fee				
	(first 30 sheets)	b1	382		
12-4	Remaining sheets		0		
12-5	Additional amount	(X)	9		
12-6	Total additional amount	b2	0		
12-7	b1 + b2 =	B	382		
12-8	Designation fees				
	Number of designations contained in international application		87		
12-9	Number of designation fees payable (maximum 6)		6		
12-10	Amount of designation fee	(X)	82		
12-11	Total designation fees	D	492		
12-12	PCT-EASY fee reduction	R	-117		
12-13	Total international fee (B+D-R)	I	⇨	757	
12 14	Fee for priority document				
	Number of priority documents requested		1		
12-15	Fee per document	(X)	15		
12 16	Total priority document fee	P	⇨	15	
12-17	TOTAL FEES PAYABLE (T+S+I+P)		⇨	1,858	
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12-21	Deposit account No	03-2457
12-22	Date	02 March 2001 (02 03 2001)
12-23	Name and signature	DUNNE, Elizabeth, M Elizabeth M Dunne

VALIDATION LOG AND REMARKS

13-2-2	Validation messages States	Green? More designations could be made The following States have not been designated US Please verify
		Yellow! Additional national designation added Obtain updated maintenance tables rather than using this field
13-2-6	Validation messages Contents	Yellow! The power of attorney or a copy of the general power of attorney will need to be furnished unless all applicants sign the request form
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PATENT COOPERATION TRE Y

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable item 5 below
6088-01		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/US 01/06899	02/03/2001	06/03/2000

Applicant

COLGATE-PALMOLIVE COMPANY

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18 A copy is being transmitted to the International Bureau

This International Search Report consists of a total of 2 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1 **Basis of the report**

a With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed unless otherwise indicated under this item

[ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b))

b With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application the international search was carried out on the basis of the sequence listing

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[ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2 [ ] **Certain claims were found unsearchable (See Box I)**

3 [ ] **Unity of invention is lacking (see Box II)**

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[X] the text is approved as submitted by the applicant.

[ ] the text has been established by this Authority to read as follows.

5 With regard to the **abstract**,

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[ ] the text has been established according to Rule 38 2(b) by this Authority as it appears in Box III The applicant may within one month from the date of mailing of this international search report, submit comments to this Authority

6 The figure of the drawings to be published with the abstract is Figure No _____

[ ] as suggested by the applicant.

[ ] because the applicant failed to suggest a figure

[ ] because this figure better characterizes the invention

[ ] None of the figures.

Form PCT/ISA/210 (first sheet) (July 1998)

INTERNATIONAL SEARCH REPORT

International Application No
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A CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K7/18 A61K7/16

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
WPI Data

C DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication where appropriate of the relevant passages	Relevant to claim No.
X	WO 99 55297 A (COLGATE-PALMOLIVE COMPANY) 4 November 1999 (1999-11-04) the whole document	1-12

☐ Further documents are listed in the continuation of box C

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X document of particular relevance the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
19 September 2001	25/09/2001

Name and mailing address of the ISA	Authorized officer
European Patent Office P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Alvarez Alvarez, C

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INTERNATIONAL SEARCH REPORT

Information on patent family members

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PCT/US 01/06899

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9955297 A	04-11-1999	AU 3666999 A	16-11-1999
		BR 9909974 A	26-12-2000
		CN 1307466 T	08-08-2001
		EP 1076550 A1	21-02-2001
		WO 9955297 A1	04-11-1999

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(54) Title: DUAL COMPONENT DENTIFRICE COMPOSITION FOR FLUORIDATING TEETH

(57) Abstract

A method is disclosed for enhancing fluoride availability using an acidulated two component dentifrice system in which the first component contains sodium fluoride and a silica abrasive in an alkaline environment and the second component contains an acid a phosphate ion source, and a silica abrasive

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Published
With international search report
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments

(54) Title DUAL COMPONENT DENTIFRICE COMPOSITION FOR FLUORIDATING TEETH

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A method is disclosed for enhancing fluoride availability using an acidulated two component dentifrice system in which the first component contains sodium fluoride and a silica abrasive in an alkaline environment and the second component contains an acid a phosphate ion source, and a silica abrasive

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DUAL COMPONENT DENTIFRICE COMPOSITION FOR FLUORIDATING TEETH

Background Of The Invention

1 Field of the Invention

This invention is directed to a dentifrice composition containing acidulated fluoride compounds effective as anticaries agents and more particularly to an acidulated phosphate fluoride dual component dentifrice composition for fluoridating teeth

2 The Prior Art

It has long been known to include fluoride containing compounds in dentifrices as anticaries agents and it has been established that these compounds are effective to reduce the incidence of dental caries Fluoride compounds which are deemed to be the most effective are sodium fluoride sodium monofluorophosphate and stannous fluoride The fluoride compounds are effective mainly due to the fluoride ions which improve the acid resistance of tooth enamel and accelerate remineralization (i e recalcification) of decayed teeth in their early stage when the decalcification has proceeded only slightly The effect of improving the acid resistance of the enamel is believed to be due to the fact that the fluoride ions are incorporated into a crystal lattice of hydroxyapatite which is the main constituent of tooth enamel or in other words, fluoride ions partially fluoridate hydroxyapatite and simultaneously repair the lattice irregularities

The effectiveness of fluoride treatment in providing acid resistance to tooth enamel is dependent upon the amount of fluoride ion which is available for deposition on the enamel being treated Also using phosphate buffered NaF the incorporation of fluoride as CaF_2 into dental enamel is facilitated at lower pH levels which increase enamel solubility Prencipe et

al , Colloid & Surface Chemistry 4th Chemical Congress of America NY (Aug 25-30 1991) It is, therefore, desirable to formulate an acidulated phosphate fluoride dentifrice to enhance fluoride deposition onto and uptake into the tooth enamel

Acidulated phosphate fluoride is disclosed in U S Patents 4,080 440 and 5 603,992 as delivered in a dual component dentifrice comprised of a separately housed first acidic component containing a fluoride salt such as NaF which with a second separately housed cationic calcium ion containing component forms the two component dentifrice for tooth remineralization While these two separately housed component formulations avoid any reactions between ingredients within the first and second components a reaction occurs within the first component between the acid sodium fluoride and silica abrasive reducing the bioavailability of the fluoride ion Although amorphous silica, generally used as an abrasive ingredient in dentifrices is one of the most chemically inert abrasives available the negatively charged oxygen atoms of the silica are protonated in the acid environment, and the resulting hydroxyl (OH) moieties hydrogen bond to the available fluoride ions released from sodium fluoride This fluoride-OH bond occurs in the acidulated phosphate fluoride silica abrasive systems disclosed in prior art Patents 4,080,440, and 5603,992 whereby the availability of the fluoride ions present in the dentifrice to fluoridate the enamel upon application thereto is significantly reduced The magnitude of this reduction in available fluoride is hereinafter demonstrated

Thus there is a clear need to formulate a stable, acidulated phosphate fluoride dentifrice having the maximum deliverable fluoride

SUMMARY OF THE INVENTION

In accordance with the present invention there is provided a method for the fluoridation of tooth enamel using a multicomponent dentifrice comprised of two separately housed semi-solid aqueous components, the first component containing sodium fluoride as a source of fluoride ions in an orally acceptable vehicle having a pH of at least about 7 5 and the second component containing both a source of phosphate ions and an acid

to provide a pH of from about 2 5 to about 5 0 in an orally acceptable vehicle each component containing a siliceous abrasive whereby upon mixing of the components a mixture having a pH of from about 4 0 to about 6 0 is formed whereby upon application of the mixture to the teeth the availability of fluoride ions is enhanced

There has been no recognition in the prior art of the significant loss of fluoride availability during extended periods of storage, resulting from the interaction of generally inert silica abrasives with sodium fluoride when NaF is present as the fluoride source in dentifrices having an acid environment In accordance with the present invention as will be further demonstrated herein the enhanced fluoride availability resulting from separating the acid and the fluoride in separate dentifrice components each containing a silica abrasive is unexpected and significant.

Description Of The Preferred Embodiments

In use the components of the two component dentifrice of the present invention comprise a first sodium fluoride and silica abrasive containing dentifrice component, and a second acid and silica abrasive containing dentifrice component these two components are preferably combined in approximately equal weight proportions so that about one-half of the concentration of any particular ingredient within either component will be present when the components are combined and applied to the teeth as by brushing Both components are formulated to provide similar apparent physical characteristics, so that the two components are simultaneously delivered in the desired predetermined amounts by extrusion from a multicompartmented tube or pump device

Dentifrice Vehicle Common to Both Components

In the preparation of the individual dentifrice components of the present invention the respective sodium fluoride or acid is incorporated within a dentifrice vehicle suitable for use in the oral cavity which contains

water humectant surfactant and a polishing agent or abrasive The humectant is generally a mixture of humectants such as glycerol sorbitol and polyethylene glycol of a molecular weight in the range of 200-1000 but other mixtures of humectants and single humectants may also be employed The humectant content within each of the two components is in the range about of 20% to about 50% by weight and preferably about 30 to about 45% by weight. The water content is from about 20% to about 45% and preferably about 30 to about 42% by weight

Surface active agents or surfactants may be incorporated in the vehicle of the individual components of the present invention as an ingredient to aid in the thorough dispersion of the dentifrice throughout the oral cavity when applied thereto as well as to improve the dentifrice s cosmetic acceptability and the foaming properties Anionic surfactants are preferred in the first, sodium fluoride containing component. Nonionic surfactants are preferred in the second acid containing component

Examples of suitable anionic surfactants for use in the first component of the present invention include water soluble salts of the higher alkyl sulfates or sulfoacetate such as sodium lauryl sulfate sodium lauryl sulfoacetate or other suitable alkyl sulfates or sulfoacetates having 8 to 18 carbon atoms in the alkyl group water soluble salts of sulfonated monoglycerides of higher fatty acids such as sodium coconut monoglyceride sulfonate or other suitable sulfonated monoglyceride of a fatty acid of 10 to 18 carbon atoms sodium lauryl phosphate salts of amides of higher fatty acid, e g , 12 to 16 carbon atom acids with lower aliphatic amino acids e g taurine or sarcosine or other amino acid of 2 to 6 carbon atoms such as sodium-N-methyl-N-palmitoyl tauride sodium N-lauroyl- N-myristoyl- and N-palmitoyl sarcosinates water soluble salts of the esters of such fatty acids with isethionic acid or with glycerol monosulfate such as the sodium salt of monosulfated monoglyceride of hydrogenated coconut oil fatty acids, water soluble salts of olefin sulfonates e g alkene sulfonates or hydroxyalkene sulfonates or mixtures thereof having 12 to 16 carbon atoms in the carbon chain of the molecule and water soluble soaps of higher fatty acids such as those of 12 to 18 carbon atoms e g. coconut fatty acids

Examples of suitable nonionic surfactants for use in the second component of the present invention include condensates of sorbitan esters of fatty acids with ethylene oxide (polysorbates) such as sorbitan monooleate with from about 20 to about 60 moles of ethylene oxide A particularly preferred polysorbate is Polysorbate 20 polyoxyethylene 20 sorbitan monolaurate marketed by ICI Newcastle Delaware 19720

Additional suitable nonionic surfactants useful in the second component of the present invention are the condensation products of an alpha-olefin oxide containing 10 to 20 carbon atoms a polyhydric alcohol containing 2 to 10 carbon atoms and 2 to 6 hydroxyl groups and either ethylene oxide or a mixture of ethylene oxide and propylene oxide The resultant surfactants are polymers which have a molecular weight in the range from about 400 to about 1600 contain from about 40% to about 80% ethylene oxide by weight, and have an alpha-olefin oxide to polyhydric alcohol mole ratio in the range from about 1 1 to about 1 3 respectively Other nonionic surfactants useful in the present invention include condensates of sorbitan esters of fatty acids with polyethylene glycol such as sorbitan diisostearate condensed with polyethylene glycol

The surface active agent can be present in one or both components of the compositions of the present invention, at a concentration of about 0 1 to about 5 0% by weight preferably about 0 2 to about 1 5% by weight of the particular component.

Siliceous abrasive materials useful in the practice of the invention include preferred silicas which have a mean particle size up to about 20 microns including a precipitated amorphous hydrated silica such as Zeodent 115, marketed by J M Huber Chemicals Division Havre de Grace Maryland 21078 or Sylodent 783 marketed by Grace Davidson Baltimore Maryland 21203

The silica abrasive is present in each of the two dentifrice components of the present invention at a concentration from about 5 to about 30% by weight, and preferably about 5 to about 20% by weight of the respective component

Fluoride Source Containing Component

The first component of the dentifrice composition of the present invention contains sodium fluoride, as the source of fluoride ions The sodium fluoride is incorporated in the first component at a concentration of about 0 1 to about 3 0% by weight and preferably at about 2 0 to about 2 5% by weight. At these preferred concentrations about 4 500 ppm to over 5 600 ppm fluoride ion will be available in solution when the combined first and second components of the dentifrice composition are admixed and applied to the teeth

It is also critical to the practice of the present invention that the first component be maintained at a pH of at least about 7 5 and preferably at a pH of at least about 8 0 Applicants' have discovered that NaF is stable in the presence of the siliceous abrasive only in a neutral or basic pH environment. A buffering agent, such as sodium hydroxide and sodium bicarbonate or sodium phosphate may be employed to adjust the pH of the fluoride ion containing dentifrice component to the desired basic levels if necessary

Acid Containing Component

The second component of the dentifrice composition of the present invention, which is maintained physically separate from the first component until mixing before use contains an acid or mixture of acids to acidulate the dentifrice when the two components are mixed prior to use Acidic compounds which can be present in the second component include both mineral and organic acids, such as, sulfuric acid hydrochloric acid malic acid alginic acid citric acid, succinic acid lactic acid tartaric acid potassium bitartrate, acid sodium citrate phosphoric acid, and sodium acid

phosphate Acid phosphates are preferred including phosphoric acid or salts of phosphoric acid containing the radical PO_4 as such acids or acid salts thereof such as sodium phosphate monobasic not only provide the necessary acidity but also provide phosphate ions to inhibit any tooth enamel demineralization which may occur with the application of the two component acidulated dentifrice to the teeth Further the combination of an acid such as phosphoric acid and an acid salt, such as sodium phosphate monobasic provides enhanced buffering to achieve the desired pH upon the mixing of the dentifrice components The preferred acid phosphoric acid is commercially available as a liquid at 85% concentration and the preferred sodium phosphate monobasic is commercially available as a monohydrate powder

The acid is incorporated in the second component of the dentifrice composition of the present invention in a total concentration of about 0 7% to about 4% by weight and preferably at about 2 0 to about 3 0% by weight, the amount being sufficient to obtain a pH of from about 2 5 to about 5 0 and preferably from about 3 5 to about 4 5

The concentration of phosphate ions within the second component of the present invention is at least about 0 05 M with a concentration of at least about 0 2 M preferred

Other Ingredients Common to Both Components

Inorganic or organic thickeners may be included in the both of the components of the dentifrice of the present invention Organic thickeners such as natural and synthetic gums and colloids may also be incorporated in the present invention Examples of such organic thickeners include carrageenan (Irish moss) xanthan gum and sodium carboxymethyl cellulose starch polyvinylpyrrolidone hydroxyethylpropyl cellulose hydroxybutyl methyl cellulose, hydroxypropylmethyl cellulose and hydroxyethyl cellulose Inorganic thickeners include amorphous silica compounds which function as thickening agents such as colloidal silicas

compounds available under tradenames such as Cab-o-sil fumed silica manufactured by Cabot Corporation and distributed by Lenape Chemical Bound Brook, New Jersey, Zeodent 165 from J M Huber Chemicals Division, Havre de Grace Maryland 21078 and Sylox 15 from Grace Davidson, Baltimore Maryland 21203 A combination of inorganic and organic thickening agents are preferred and may be present in both components of the instant dentifrice in proportions of about 0 5 to about 15% by weight, preferably about 0 8 to about 6% in each of the two dentifrice components

A striped dentifrice product may be obtained using the multicomponent dentifrice of the present invention wherein colorants of contrasting colors are incorporated in each of the dentifrice components to be dispensed the colorants being non-toxic when used in the suggested amounts Colorants used in the practice of the present invention include both pigments and dyes

Pigments used in the practice of the present invention include non-toxic, water insoluble inorganic pigments such as titanium dioxide (TiO_2) and chromium oxide greens, ultramarine blues and pinks and ferric oxides Dyes include water insoluble dye lakes prepared by extending calcium or aluminum salts of FD&C dyes on alumina such as FD&C Green #1 lake FD&C Blue #2 lake FD&C R&D #30 lake and FD&C # Yellow 15 lake The concentration of the pigment or dye in the dentifrice composition ranges in amount from about 0 0005 percent to about 2 percent by weight of the respective component

Other ingredients which may be incorporated in one or both components of the present invention include antibacterial agents antitartar actives sweetener flavor and preservatives, such as sodium benzoate

Preferred antibacterial agents are non-cationic antibacterial agents based on phenolic and bisphenolic compounds, halogenated diphenyl ethers such as triclosan benzoate esters and carbanilides Cationic antibacterial agents which are also preferred including quaternary ammonium salts

such as chlorhexidine digluconate can only be included in the second acid containing component of the present invention Such antibacterial agents can be present in quantities of from about 0 03 to about 1% by weight of the particular component

Antitartar actives such as sodium tripolyphosphate tetrapotassium or tetrasodium pyrophosphates, or mixtures thereof can be present in concentrations from about 0 5 to about 8% by weight of the particular component in which such actives are stable The sweetener content will normally be that of an artificial or synthetic sweetener and the normal proportion thereof present will be in the range of 0 1 to 1% by weight of the respective component, preferably 0 2 to 0 5% by weight the respective component. The flavor content which is preferably a fruit or mixed peppermint/menthol flavor will usually be in the range of 0 5 to 2% by weight of the respective component, preferably 0 5 to 1 0% by weight of the respective component The contents of other components or adjuvants will normally not exceed 10% by weight, often will be less than 5% by weight and can be as low as 0%

When noncationic antibacterial agents are included in any of the dentifrice components there is also preferably included from about 0 05 to about 5% of an antibacterial enhancing agent (AEA) which enhances the delivery and retention of the noncationic antibacterial agent to, and retention thereof on oral surfaces AEA s useful in the present invention are disclosed in U S Patents 5 188 821 and 5 192 531 and include synthetic anionic polymeric polycarboxylates in the form 1 4 to 4 1 copolymers of maleic anhydride or acid with another polymerizable ethylenically unsaturated monomer preferably methyl vinyl ether/maleic anhydride having a molecular weight (M W) of about 30,000 to about 1 000 000 most preferably about 30,000 to about 800,000 These copolymers are available for example as Gantrez e g AN 139 (M W 500 000) AN 119 (M W 250 000) and preferably S-97 Pharmaceutical Grade (M W 700 000) available from ISP Technologies, Inc Bound Brook, N J 08805

Preparation of the Dentifrice

To prepare either of the dentifrice components of the present invention generally the humectants e g glycerin propylene glycol polyethylene glycol ingredients are dispersed with any sweetener and water in a conventional mixer until the mixture becomes a homogeneous gel phase Into the gel phase are added a pigment such as TiO_2 any antibacterial agent such as triclosan, any antibacterial enhancing agent such as Gantrez any tartar control agents such as tetrasodium pyrophosphate or sodium tripolyphosphate or both in the second component the acid phosphate, and in the first component the fluoride ion source i e sodium fluoride These ingredients are mixed until a homogenous phase is obtained Thereafter the thickener silica abrasive flavor and surfactant ingredients are added and the ingredients mixed at high speed under vacuum of from about 20 to 100 mm of Hg The resultant product is in the case of each component is a homogeneous, semi-solid extrudable paste product.

Packaging of the Dentifrice

The multicomponent dentifrice composition of the present invention is packaged in a suitable dispensing container in which the components are maintained physically separated and from which the separated components may be dispensed synchronously as a ribbon for application to a toothbrush Such containers are known in the art. An example of such a container is a two compartment dispensing container, such as a pump or tube, having collapsible sidewalls, as disclosed in U S Patents 4 487,757 and 4 687,663, wherein the container body is formed from a collapsible plastic web and is provided with a partition within the container body defining separate compartments in which the physically separated components are stored and from which they are dispensed through a suitable dispensing outlet.

The following example is further illustrative the present invention but it is understood that the invention is not limited thereto All amounts and proportions referred to herein and in the appended claims are by weight unless otherwise stated

Example

A two component dentifrice of the present invention was prepared designated Toothpaste I having a first sodium fluoride and silica abrasive containing component and a second acid phosphate and silica abrasive containing component. The ingredients and pH of each of the two components of Toothpaste I are itemized in Table I below

Table I

Toothpaste I

Ingredients	1st Component (in weight %)	2nd Component (in weight %)
PEG 600	3 00	3 00
Xanthan Gum	0 80	0 80
Sorbitol	37 15	36 58
Water	39 24	38 24
Sodium fluoride*	2 21	-----
Sodium benzoate	0 50	0 50
Phosphoric Acid 85%	-----	0 96
Sodium phosphate monobasic	-----	1 82
Sodium saccharin	0 25	0 25
Dye	0 50	0 50
Sylox 15	10 0	10 0
Zeodent 115	5 35	5 35
Polysorbate 20	-----	0 50
Sodium Lauryl Sulfate	1 0	----
Flavor	0 50	0 50
Total %	100%	100%
Ph	8 0	3 5

**Contains potentially 5000 ppm releasable F^- with combination of 1st and 2nd components upon admixing prior to application to the dentiture*

To determine the fluoride ion availability of the multicomponent dentifrice of the present invention after storage for a period of 8 weeks the 1st and 2nd components of Toothpaste I were mixed together diluted one-thousand times using a commercially available buffering solution (Orion TISAB II) at ambient room temperature the available fluoride ion concentration was determined using a Corning Model 350 pH/ion Analyzer Corning Inc , Corning N Y equipped with a Orion Fluoride Electrode Model #94-09 Orion Research Products, Boston Mass The EMF output from the Orion Fluoride Electrode was converted to ppm fluoride by means of a logarithmic-linear calibration established with known concentrations of fluoride in the buffering solution and the resultant ppm of available fluoride determined has been recorded in Table III below

For purposes of comparison the procedure was repeated except the dentifrice assayed for fluoride availability was a single component acidulated phosphate fluoride dentifrice of the prior art, containing a silica abrasive designated Toothpaste II having the ingredients and pH listed in Table II below Referring to Table II note that the amount of sodium fluoride within Toothpaste II is one-half that of the 1st Component of Toothpaste I so that a comparable potential 5 000 ppm of fluoride would be delivered upon use by each After a comparable eight weeks of storage, the available soluble fluoride of Toothpaste II was assayed using the same methodology as that used for Toothpaste I and the results are also recorded in Table III below

Table II

Toothpaste II

Ingredients	Composition (in weight %)
PEG 600	3 00
Xanthan Gum	0 80
Sorbitol	34 37
Water	39 345
Sodium fluoride	1 105
Sodium benzoate	0 50
Phosphoric Acid 85%	0 96
Sodium phosphate monobasic	1 82
Sodium saccharin	0 25
Dye	0 50
Sylox 15	10 0
Zeodent 115	5 35
Polysorbate 20	0 50
Sodium Lauryl Sulfate	1 0
Flavor	0 50
Total %	100%
pH	5 0

Table III

Fluoride Availability

Toothpaste Analyzed	Available Soluble Fluoride Ion (in ppm)
Toothpaste I	4 900
Toothpaste II	3,800

Referring to Table III, the 4 900 ppm is equivalent to 98% availability of the fluoride in Toothpaste I and the 3 800 ppm is correspondingly equivalent to 76% fluoride availability in Toothpaste II The 22% difference in available fluoride between Toothpaste I of the present invention and

comparative Toothpaste II is significant and unexpectedly large The magnitude of the loss of available fluoride in Toothpaste II is at a level of significance rendering Toothpaste II commercially unacceptable

7-2

Claims

What is claimed is

1 A method for the fluoridation of teeth utilizing a two component dentifrice system comprising the steps of (1) preparing a first dentifrice component containing sodium fluoride as the fluoridation source and having a pH of at least about 7 5, and a second dentifrice component containing a source of phosphate ions and an acid in an amount sufficient to maintain the pH in the range of about 2 5 to about 5 0 both dentifrice components containing a siliceous abrasive (2) maintaining the first and second dentifrice components separate from the other until application to teeth requiring fluoridation (3) mixing the first and second components together to form a mixture having a pH of from about 4 0 to about 6 0 (4) applying the mixture to the teeth, whereby enhanced availability of fluoride ions to tooth enamel is observed

2 The method of claim 1 wherein the source of phosphate ions is phosphoric acid sodium phosphate monobasic or a combination thereof

3 The method of claim 1, wherein the first component contains from about 0 1 to about 3 0% by weight sodium fluoride

4 The method of claim 1, wherein the second component contains from about 0 7 to about 4% by weight of an acid phosphate and an acid salt

5 The method of claim 4 wherein the acid phosphate is phosphoric acid and the acid salt is sodium phosphate monobasic

6 The method of claim 1 wherein the pH of the first component is at least about pH 8 0

7 The method of claim 1 wherein the acid is in an amount sufficient to maintain the pH of the second component in the range of about pH 3 5 to about pH 4 5

8 The method of claim 1 wherein the siliceous abrasive is a precipitated amorphous hydrated silica

9 The method of claim 8 wherein the dentifrice composition contains from 10 to 30% in total of the amorphous hydrated silica abrasive

10 The method of claim 9 wherein both components of the dentifrice system each contain 15 35% by weight of the amorphous hydrated silica abrasive

11 The method of claim 1, wherein a surfactant is incorporated in both components of the dentifrice system

12 The method of claim 11, wherein the surfactant incorporated in the first component of the dentifrice system is sodium lauryl sulfate and the surfactant incorporated in the second component of the dentifrice is a condensate of sorbitan esters of fatty acids with ethylene oxide

INTERNATIONAL SEARCH REPORT

Ir ational Application No
PCT/US 99/09108

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K7/16 A61K7/18

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication where appropriate, of the relevant passages	Relevant to claim No
A	US 5 071 637 A (PELLICO MICHAEL A) 10 December 1991 (1991-12-10) claims, examples	1-5,7, 11,12
P,A	WO 98 22079 A (PROCTER & GAMBLE) 28 May 1998 (1998-05-28) claims 1-5,8, examples	1-12
A	FR 8 273 M (THE KENDALL CO) 7 December 1970 (1970-12-07) claims	1-12
A	WO 97 46216 A (COLGATE PALMOLIVE CO) 11 December 1997 (1997-12-11) abstract, claims	1

☐ Further documents are listed in the continuation of box C

☒ Patent family members are listed in annex.

* Special categories of cited documents

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed
- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- & document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
19 August 1999	26/08/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P B 5818 Patentlaan 2 NL 2280 HV Rijswijk Tel. (+31 70) 340-2040, Tx. 31 651 epo nl, Fax (+31 70) 340-3016	Pelli Wablat, B

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 99/09108

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5071637 A	10-12-1991	US 5073363 A	17-12-1991
WO 9822079 A	28-05-1998	AU 5202398 A	10-06-1998
FR 8273 M	26-10-1970	DE 1804275 A	14-05-1969
		FR 1590023 A	06-04-1970
		GB 1188914 A	22-04-1970
		SE 350193 B	23-10-1972
		US 3510553 A	05-05-1970
WO 9746216 A	11-12-1997	US 5785956 A	28-07-1998
		AU 3080197 A	05-01-1998
		CA 2253517 A	11-12-1997
		EP 0912161 A	06-05-1999

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
IR 6088-01		
International application No	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US01/06899	02/03/2001	06/03/2000
International Patent Classification (IPC) or national classification and IPC A61K7/18		
Applicant COLGATE PALMOLIVE COMPANY		

1 This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36

2 This REPORT consists of a total of 4 sheets including this cover sheet

☐ This report is also accompanied by ANNEXES i e sheets of the description claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70 16 and Section 607 of the Administrative Instructions under the PCT)

These annexes consist of a total of sheets

3 This report contains indications relating to the following items.

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☐ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability citations and explanations suporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
24/09/2001	28.06.2002
Name and mailing address of the international preliminary examining authority European Patent Office D-80298 Munich Tel +49 89 2399 0 Tx 523656 epmu d Fax +49 89 2399 4465	Authorized officer Paloniemi Legland, R Telephone No +49 89 2399 7315

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No PCT/US01/06899

I Basis of the report

1 With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70 16 and 70 17))*
Description, pages

1-15 as originally filed

Claims, No

1-12 as originally filed

2 With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed unless otherwise indicated under this item

These elements were available or furnished to this Authority in the following language , which is

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23 1(b))
- ☐ the language of publication of the international application (under Rule 48 3(b))
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55 2 and/or 55 3)

3 With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing

- ☐ contained in the international application in written form
- ☐ filed together with the international application in computer readable form
- ☐ furnished subsequently to this Authority in written form
- ☐ furnished subsequently to this Authority in computer readable form
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

4 The amendments have resulted in the cancellation of

- ☐ the description, pages
- ☐ the claims, Nos
- ☐ the drawings, sheets

5 ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70 2(c))

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 1-12 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67 1(iv) PCT Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT)

For the assessment of the present claims 1-12 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States The patentability can also be dependent upon the formulation of the claims The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment

Therefore no examination under Art 33(1), i e novelty, inventive step and industrial applicability will be carried out for these claims (1-12)

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To

Shapiro, Paul
COLGATE-PALMOLIVE COMPANY
909 River Road
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ETATS-UNIS D'AMERIQUE

PCT

WRITTEN OPINION

(PCT Rule 66)

77

Date of mailing *(day/month/year)*	22 04 2002
Applicant's or agent's file reference: IR 6088-01	REPLY DUE: within 3 month(s) from the above date of mailing

International application No	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US01/06899	02/03/2001	06/03/2000

International Patent Classification (IPC) or both national classification and IPC

A61K7/18

Applicant

COLGATE-PALMOLIVE COMPANY

1 This written opinion is the second drawn up by this International Preliminary Examining Authority

2 This opinion contains indications relating to the following items.

- I ☒ Basis of the opinion
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☐ Reasoned statement under Rule 66 2(a)(ii) with regard to novelty inventive step or industrial applicability citations and explanations supporting such statement
- VI ☐ Certain document cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

3 The applicant is hereby invited to reply to this opinion

When? See the time limit indicated above The applicant may before the expiration of that time limit, request this Authority to grant an extension see Rule 66.2(d)

How? By submitting a written reply accompanied where appropriate by amendments according to Rule 66.3 For the form and the language of the amendments see Rules 66.8 and 66 9

Also For an additional opportunity to submit amendments see Rule 66.4. For the examiner's obligation to consider amendments and/or arguments see Rule 66.4 bis. For an informal communication with the examiner see Rule 66.6

If no reply is filed the international preliminary examination report will be established on the basis of this opinion

4 The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 06/07/2002

Name and mailing address of the international preliminary examining authority:
European Patent Office
D-80298 Munich
Tel +49 89 2399 0 Tx 523656 epmu d
Fax +49 89 2399 4465

Authorized officer / Examiner
Paloniemi Legland, R

Formalities officer (incl extension of time limits)
Christensen, J
Telephone No +49 89 2399 8052

I **Basis of the opinion**

1 With regard to the **elements** of the international application (Replacement *sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed"*)

Description, pages

1-15 as originally filed

Claims, No

1-12 as originally filed

2 With regard to the **language** all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item

These elements were available or furnished to this Authority in the following language which is

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23 1(b))
- ☐ the language of publication of the international application (under Rule 48 3(b))
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55 2 and/or 55 3)

3 With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application the international preliminary examination was carried out on the basis of the sequence listing

- ☐ contained in the international application in written form
- ☐ filed together with the international application in computer readable form
- ☐ furnished subsequently to this Authority in written form
- ☐ furnished subsequently to this Authority in computer readable form
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

4 The amendments have resulted in the cancellation of

- ☐ the description, pages
- ☐ the claims, Nos
- ☐ the drawings sheets

5 ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70 2(c))

(Any replacement sheet containing such amendments must be referred to under Item 1 and annexed to this report)

6 Additional observations, if necessary

III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1 The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious) or to be industrially applicable have not been and will not be examined in respect of

☐ the entire international application,

☒ claims Nos 1-12 concerning industrial applicability,

because

☒ the said international application, or the said claims Nos 1-12 relate to the following subject matter which does not require an international preliminary examination (*specify*)
see separate sheet

☐ the description claims or drawings (*indicate particular elements below*) or said claims Nos are so unclear that no meaningful opinion could be formed (*specify*)

☐ the claims or said claims Nos are so inadequately supported by the description that no meaningful opinion could be formed

☐ no international search report has been established for the said claims Nos

2 A written opinion cannot be drawn due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions

☐ the written form has not been furnished or does not comply with the standard

☐ the computer readable form has not been furnished or does not comply with the standard

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 1-12 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67 1(iv) PCT Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT)

For the assessment of the present claims 1-12 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States The patentability can also be dependent upon the formulation of the claims The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment

Therefore no examination under Art 33(1), i e novelty, inventive step and industrial applicability will be carried out for these claims (1-12)

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Dependencia: 2020 DIVISION DE NUEVAS CREACIONES

Industria y Comercio
SUPERINTENDENCIA

REQUISITOS NECESARIOS PARA PRESENTACION Y AGILIZACIÓN DEL TRAMITE

	USUARIO	RADICADOR
PATENTE DE INVENCIÓN [✓] **MODELO DE UTILIDAD**	[ ]	[✓]
• Indicación de que se solicita la concesión de una patente	[ ]	[✓]
• Datos de identificación del solicitante o de la persona que presenta la solicitud	[ ]	[✓]
• Descripción de la invención	[ ]	[✓]
• Dibujos de ser estos pertinentes	[ ]	[✓]
• Comprobante de Pago de las tasas establecidas	[ ]	[ ]
COMPLETA [✓] **INCOMPLETA**	[ ]	[ ]
DISEÑO INDUSTRIAL [ ]		
• Indicación de que se solicita el registro de Diseño Industrial	[ ]	[ ]
• Datos de identificación del solicitante o de la persona que presenta la solicitud	[ ]	[ ]
• Representación gráfica y fotográfica del Diseño Industrial o muestra del material que incorpora el diseño	[ ]	[ ]
• Comprobante de pago de las tasas establecidas	[ ]	[ ]
COMPLETA [ ] **INCOMPLETA**	[ ]	[ ]
ESQUEMA DE TRAZADO [ ]		
• Indicación de que se solicita el registro de un Esquema de trazado	[ ]	[ ]
• Datos de identificación del solicitante o de la persona que presenta la solicitud	[ ]	[ ]
• Representación gráfica del esquema de trazado	[ ]	[ ]
• Comprobante de pago de las tasas establecidas.	[ ]	[ ]
COMPLETA [ ] **INCOMPLETA**	[ ]	[ ]

Firma Responsable

Fecha:_____

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