

Q.F.

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



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División de Nuevas Creaciones

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54. TITULO COMPOSICION ORAL ESTABLE, ANTIPLACA, QUE COMPRENDE UN COMPUESTO
ESTER ANTIBACTERIANO DERIVADO DE ARGININA

51. CLASIFICACION INTERNACIONAL

71. SOLICITANTE COLGATE - PALMOLIVE COMPANY

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74. APODERADO JUAN PABLO CADENA SARMIENTO

22. SANTAFE DE BOGOTA, D.C.

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☐ Patente de Modelo de Utilidad.

☒ Capítulo I.

☐ Capítulo II.

2

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4

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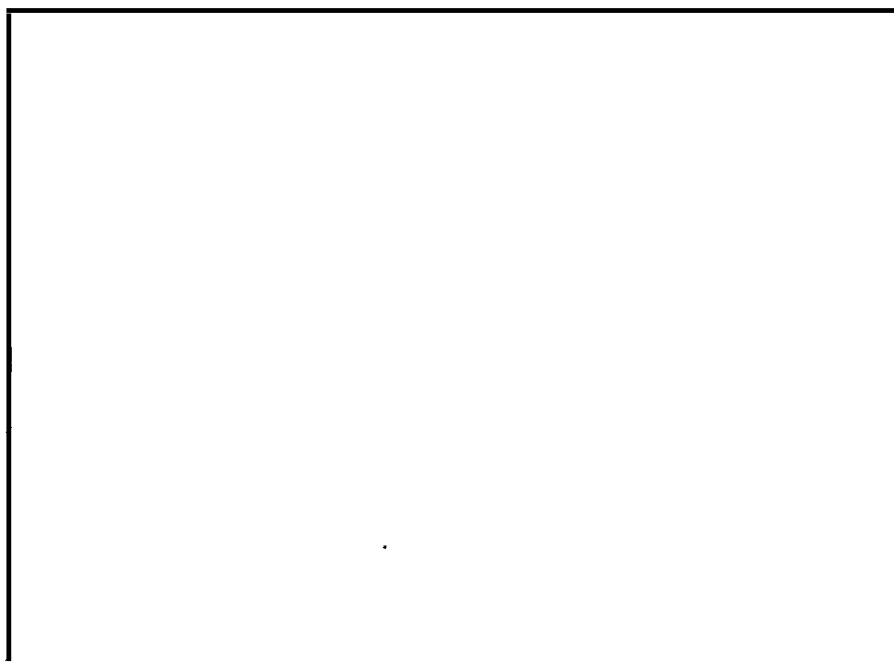
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ANEXOS

- ☒ Comprobante de pago de la tasa de presentación de la solicitud. \$443.000
- ☒ Documento que acredite la existencia y representación legal cuando el solicitante sea persona jurídica.
- ☒ Poderes, si fuere el caso **Fotocopia autenticada**
- ☒ Documento de cesión del inventor al solicitante o a su causante
- ☐ Declaraciones
- ☒ Copia de la solicitud internacional (Resumen, descripción, reivindicaciones, dibujos)
- ☒ Traducción de la solicitud internacional al castellano. (Resumen, descripción, reivindicaciones, dibujos)
- ☐ 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
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- ☐ 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 Tarjeta de Propietarios
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12 Solicito la concesión de la patente,

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ning of each regular issue of the PCT Gazette.

(54) Title: STABLE DENTIFRICE COMPOSITIONS

(57) Abstract: A cationic-compatible inorganic particulate comprising silica substantially coated with a non-ionic surfactant, such as an ethoxylated hydrogenated hydrocarbon oil. Compositions comprising the cationic-compatible particulate and a cationic active, such as cetyl pyridinium chloride or an ethyl lauryl arginine ester, are also provided.

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STABLE DENTIFRICE COMPOSITIONS

BACKGROUND

[0001] The present invention relates to an oral care composition which contains an inorganic particulate component in an oral care composition, and more particularly to a dentifrice composition containing a cationic-compatible inorganic particulate component with an oral care active antibacterial compound, which achieves plaque reduction with superior breath freshening characteristics.

[0002] Halitosis, the technical term for bad breath, or *Fetor ex Oris*, is an undesirable condition. As a matter of fact, everyone, excluding the very young, occasionally has bad breath, with approximately 25% suffering on a regular basis and the problem tends to get worse and more frequent as one gets older. The problem seems to be evenly split between men and women. Bad breath results when proteins from the food we eat and saliva debris are broken down by bacteria. Even the cleanest mouth hosts millions of bacteria which have the potential to decompose these protein-containing particles left in the mouth. This bacterial population forms foul smelling products, called volatile sulfur compounds (VSC) - such as hydrogen sulfide ("rotten eggs") and methyl mercaptans ("skunk smell") and other odorous and bad tasting compounds. Up to 80-90% of bad breath that originates in the mouth is by this mechanism.

[0003] Dental plaque or plaque bio-film is a soft deposit that forms on teeth and is comprised of an accumulation of bacteria and salivary as well as food by-products. Plaque adheres tenaciously at the points of irregularity or discontinuity, e.g., on rough calculus surfaces, at the gum line, on tongue surface and within crevices, and the like. Besides being unsightly, plaque is implicated in the occurrence of gingivitis and other forms of periodontal disease.

[0004] A wide variety of antibacterial agents have been suggested in the art to retard plaque formation and the oral infections and dental disease associated with plaque formation. For example US 5,874,068 and GB 1352420 disclose that arginine derivative compounds exhibit antibacterial activity when used in oral compositions such as mouthrinses to counter plaque formation by bacterial accumulation in the oral cavity. Arginine derivative compounds and their salts in particular show excellent inhibitory effect against microorganisms which possess relatively strong resistance to bacterial such as *S. aureus*, *S. mutans*, *F. nucleatum* which are involved in plaque formation on teeth. Other cationic oral care active ingredients, such as bis biguanides or cetyl pyridinium chloride (CPC) are also known for their inhibitory effect on plaque formation and bacterial accumulation in the oral cavity.

[0005] Although the cationic active material compounds, such as for example, the arginine derivative compounds disclosed in the prior art, are effective antibacterial agents, when these compounds are included in silica containing dentifrice it was discovered that when the dentifrice was applied to the teeth, the bioavailability of the arginine derivative compound was reduced to a level whereby little antiplaque benefit was achieved. Investigation of this problem led to the discovery that compounds such as abrasives and thickeners such as silica compounds conventionally used in the preparation of dentifrice compositions were the factor responsible for the impairment of the antiplaque efficacy of the arginine derivative compound.

[0006] Thus, there is a clear need in the art to formulate a dental product capable of delivering a cationic active antiplaque antibacterial agent whereby the

ingredients used to prepare the dentifrice composition do not inhibit the bioavailability of the cationic antiplaque agent so that optimum antiplaque benefits result.

SUMMARY

[0007] In one aspect, the present invention provides a cationic-compatible inorganic component for an oral care composition comprising an inorganic particulate component comprising silica and having a surface substantially coated with a non-ionic surfactant to form the cationic-compatible inorganic component.

[0008] In another aspect the present invention provides an oral care composition comprising an active ingredient comprising a cationic compound and an inorganic particulate component having a surface substantially coated with a non-ionic surfactant.

[0009] In yet another aspect, the present invention provides a method of making a dentifrice having an enhanced availability of a cationic oral care active ingredient comprising coating an inorganic particulate component with a non-ionic surfactant to form a cationic-compatible inorganic component, and adding the cationic-compatible inorganic component into a dentifrice composition comprising a cationic oral care active compound.

[0010] It has been discovered that compositions and methods of this invention afford advantages over prior art oral care compositions using cationic antibacterial ingredients and inorganic particulates, such as those known in the art. Such advantages over the art include one or more of the following: enhanced bioavailability and efficacy of a cationic active ingredient translating to improved antibacterial and/or antiplaque efficacy, potential to reduce concentrations of cationic active materials in oral care compositions comprising an inorganic particulate, potential expansion of the active ingredients useful in dentifrice oral compositions.

Further uses, benefits and embodiments of the present invention are apparent from the description set forth herein.

DESCRIPTION

[0011] The following definitions and non-limiting guidelines must be considered in reviewing the description of this invention set forth herein. The headings (such as "Introduction" and "Summary,") and sub-headings (such as, "Cationic Active Ingredients", "Inorganic Particulate Components", "Non-Ionic Surfactant" "Additional Antimicrobial Active Ingredients", "Dentifrice Vehicle", "Surfactants" "Thickening Agents", "Flavor A gents", "Fluoride Providing Agents", "Antitartar Agents", "Other Ingredients", and "Methods") used herein are intended only for general organization of topics within the disclosure of the invention, and are not intended to limit the disclosure of the invention or any aspect thereof. In particular, subject matter disclosed in the "Introduction" may include aspects of technology within the scope of the invention, and may not constitute a recitation of prior art. Subject matter disclosed in the "Summary" is not an exhaustive or complete disclosure of the entire scope of the invention or any embodiments thereof. Classification or discussion of a material within a section of this specification as having a particular utility is made for convenience, and no inference should be drawn that the material must necessarily or solely function in accordance with its classification herein when it is used in any given composition.

[0012] The citation of any references herein does not constitute an admission that those references are prior art or have any relevance to the patentability of the invention disclosed herein. Any discussion of the content of references cited in the Introduction is intended merely to provide a general summary of assertions made by the authors of the references, and does not constitute an admission as to the

accuracy of the content of such references. All references cited in the Description section of this specification are hereby incorporated by reference in their entirety.

[0013] The description and any specific examples, while indicating embodiments of the invention, are intended for purposes of illustration only and are not intended to limit the scope of the invention. Moreover, recitation of multiple embodiments having stated features is not intended to exclude other embodiments having additional features, or other embodiments incorporating different combinations the stated of features. Specific Examples are provided for illustrative purposes of how to make and use the compositions and methods of this invention and, unless explicitly stated otherwise, are not intended to be a representation that given embodiments of this invention have, or have not, been made or tested.

[0014] As used herein, the words "preferred" and "preferably" refer to embodiments of the invention that afford certain benefits, under certain circumstances. However, other embodiments may also be preferred, under the same or other circumstances. Furthermore, the recitation of one or more preferred embodiments does not imply that other embodiments are not useful, and is not intended to exclude other embodiments from the scope of the invention.

[0015] As used herein, the word "include," and its variants, is intended to be non-limiting, such that recitation of items in a list is not to the exclusion of other like items that may also be useful in the materials, compositions, devices, and methods of this invention.

[0016] As referred to herein, all compositional percentages are by weight of the total composition, unless otherwise specified.

[0017] As referred to herein, the word "substantially," when applied to a characteristic of a composition or method of this invention, indicates that there may

be variation in the characteristic without having substantial effect on the chemical or physical attributes of the composition or method.

[0018] As used herein, the term "about," when applied to the value for a parameter of a composition or method of this invention, indicates that the calculation or the measurement of the value allows some slight imprecision without having a substantial effect on the chemical or physical attributes of the composition or method. If, for some reason, the imprecision provided by "about" is not otherwise understood in the art with this ordinary meaning, then "about" as used herein indicates a possible variation of up to 5% in the value.

Inorganic Particulate Components

[0019] The present invention provides cationic-compatible inorganic components for an oral care composition, said components comprising an anionic particulate substantially coated with a non-ionic surfactant. Without limiting the compositions, methods or utility of the present invention, in various embodiments, the inorganic particulate components afford diminished interaction between cationic active compounds (discussed below) and silica relative to the interaction between such materials that would occur in a prior art aqueous composition, thus optimizing the bioavailability of the cationic active compounds.

[0020] Anionic particulates among those useful herein include silica, alumina, or both. In one embodiment, the inorganic component material comprises silica. Silica abrasives useful in the practice of the present invention include silica gels and precipitated amorphous silicas. These silicas are colloidal particles/particulates having an average particle size ranging from about 3 microns to about 12 microns, and more preferably between about 5 to about 10 microns and a pH range from 4 to 10 preferably 6 to 9 when measured as a 5% by weight slurry.

[0021] Illustrative of silica abrasives useful in the practice of the present invention are marketed under the trade designation Sylodent XWA by Davison Chemical Division of W.R. Grace & Co., Baltimore, MD 21203. Sylodent 650 XWA, a silica hydrogel composed of particulates of colloidal silica having a water content of 29% by weight averaging from about 7 to about 10 microns in diameter.

[0022] Other inorganic component abrasives used in the practice of the present invention include precipitated silicas having a mean particle size of up to about 20 microns, such as Zeodent 115, marketed by J.M. Huber Chemicals Division, Havre de Grace, Maryland 21078, or Sylodent 783 marketed by Davison Chemical Division of W.R. Grace & Company.

[0023] The silica abrasive materials may be used individually as the sole abrasive in preparing the dental composition of the present invention or in combination with other known dentifrice abrasives such as sodium metaphosphate, dihydrated dicalcium phosphate, calcined alumina. The total quantity of abrasive present in the dentifrice compositions of the present invention is at a level of from about 5% to about 60% by weight, preferably from about 10% to about 55% by weight when the dentifrice composition is a toothpaste.

[0024] Silica compounds which function as thickening agents which may be used in the practice of the present invention include colloidal silica compounds available under the trade designation Cabo-sil 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; and Sylodent 15, available from Davison Chemical Division of W.R. Grace Corporation, Baltimore, Maryland.

Non-Ionic Surfactant

[0025] In one aspect of the current invention, inorganic particulates that are otherwise incompatible with cationic antimicrobial agents are rendered compatible with the agents by treatment or reaction with a nonionic surfactant prior to their formulation in dentifrice compositions along with the cationic material. The improved compatibility is shown for example, from *in vitro* measurements of availability of the various antimicrobial agents of the compositions of the invention.

[0026] Although the invention is not to be limited by any theory of action of the non-ionic surfactant, it is believed that the reaction or treatment of the inorganic particulates with the nonionic surfactant results in the deposition or attachment of nonionic surfactant molecules to the inorganic particulates, which results in a coating of substantially all of the charged surface of the inorganic particulates. Still not to be limited by theory, the deposition or attachment may be by either physical means, chemical means, or a combination thereof. Thus, the nonionic surfactant molecules may be held or deposited on the surface of the inorganic particulates by van der Waals attractions, hydrogen bonds, the formation of covalent bonds with reactive species on the surface of the particulates, and so on. The inorganic particulates of the present invention generally have a negative charge, and are thus considered to be anionic.

[0027] On a molecular level, surface active agents (or surfactants) are understood as being made of two moieties. The first is a hydrophilic moiety and the second is a hydrophobic moiety. As is well known, surfactants "work" by interacting with one phase of material at its surface. The resulting structure mediates the interfacial interaction of the phase with other phases. An important consideration in the action of surface active agents is the relative strength of the respective hydrophilic and hydrophobic portions of the molecule. The relative strength can be expressed and

understood as a balance between the hydrophilic characteristics of one part of the molecule and the hydrophobic characteristics of another.

[0028] Nonionic surfactants are made of chemical constituents that result in a molecule having no ionic charges. As such, the nonionic surfactant are distinguished from cationic surfactants, anionic surfactants, and amphoteric surfactants. In a preferred embodiment, the hydrophilic moiety of a nonionic surfactant is based on a polyoxyalkylene structure. A polyoxyalkylene structure is a polyether type polymer that formally represents the polymerization product of a wide variety of cyclic ethers that polymerize by ring opening polymerization. Non-ionic surfactants useful in the invention are usually synthesized by the polymerization of such cyclic ethers.

[0029] Among the cyclic ethers that may be polymerized to form the hydrophilic portion of the nonionic surfactant of the invention are those having from two to eight carbon atoms, with ring structures of three to five atoms. Suitable cyclic ether systems for polymerization include oxiranes (three membered rings), oxetanes (four member rings), and furans (five-membered rings). The surfactants may be made by homo or copolymerization of one or more of such cyclic ethers. In a preferred embodiment, oxiranes are polymerized under basic catalysis, followed by neutralization of the polymeric product. Polyoxyalkylene or polyether hydrophilic moieties may also be produced by acid catalyzed polymerization of cyclic ethers.

[0030] The size and relative proportion of alkylene groups in the polyoxyalkylene hydrophilic moiety determines its relative hydrophilic nature. In general the hydrophilic nature is related to the proportion of lower cyclic ethers that are present in the polymerization mix. In a preferred embodiment, the polyoxyalkylene hydrophilic moiety of the surfactant is made of polyoxyethylene,

resulting from the polymerization of ethylene oxide. (Ethylene oxide is an oxirane containing two carbons). Relatively smaller amounts of propyleneoxide, butyleneoxide, and other higher cyclic ethers may be copolymerized with the ethylene oxide to form the hydrophilic moieties on the surfactant of the invention, as long as the balance of hydrophilic and hydrophobic character in the resulting surfactant is suitable for application in the invention.

[0031] The hydrophobic moieties on the non ionic surfactants of the invention are generally organic radicals containing at least about twelve carbons. These surfactants are made by polymerizing ethylene oxide or a mixture of alkylene oxides and/or cyclic ethers onto an organic molecule that serves as a starting material. The starting material contains at least about 12 carbon atoms, and an organic group containing an active hydrogen that will react with the cyclic ethers to form the polyoxyalkylene. Reactive organic groups containing active hydrogen include without limitation, hydroxyl, carboxyl, amine, amide, and mercaptan. A preferred reactive group is hydroxyl, whereby the starting material is an organic alcohol containing at least about 12 carbon atoms. Thus, suitable nonionic surfactants may be prepared by polymerizing ethylene oxide or a mixture of cyclic ethers onto fatty alcohols, fatty acids, fatty acid amides, and the like. Commercially available fatty alcohols, fatty acids, fatty amides and fatty amines includes those containing from about 12 to about 26 carbon atoms.

[0032] In a preferred embodiment, the hydrophobic moiety is based on hydroxyl functional diglycerides and triglycerides. Such diglycerides and triglycerides are available as vegetable oils. In a preferred embodiment, castor oil, a triglyceride containing hydroxyl functionality is used to make the nonionic surfactants of the invention. In a preferred embodiment, ethyleneoxide or a mixture of cyclic

ethers is polymerized onto castor oil until at least about 10, preferably about 20, and more preferably about 40 alkylene oxide units are added per molecule of the oil. Preferably, the extent of alkoxylation is less than 600, preferably less than 400, and more preferably less than 200. The castor oil alkoxylate resulting from the polymerization may then be hydrogenated by conventional means to form a hydrogenated castor oil alkoxylate. Alternatively, the castor oil, which in its native form contains olefinic unsaturation, may be hydrogenated prior to the reaction of the hydroxyl functional oil with the cyclic ethers. Thus, in a preferred embodiment, the nonionic surfactant comprises a castor oil alkoxylate or a hydrogenated alkoxylate having from about 20 to 200 repeating oxyalkylene units in the hydrophilic moiety. In a preferred embodiment, the oxyalkylene units are predominantly oxyethylene. In a particularly preferred embodiment, the polyoxyalkylene moiety is polyoxyethylene.

[0033] Ethoxylated castor oil and hydrogenated ethoxylated castor oils are known by the non-proprietary name of PEG hydrogenated castor oils, in accordance with dictionary of the Cosmetics, Toiletries and Fragrance Association, 3rd Edition which name is used in conjunction with a numeric suffix to designate the degree of ethoxylation of the hydrogenated castor oil product, i.e., the number of moles of ethylene oxide added to the hydrogenated castor oil product. Such ethoxylated and hydrogenated ethoxylated castor oils are commercially available and are commonly designated as PEG NN castor oil or PEG NN hydrogenated castor oil, where NN designates the number of ethylene oxide units polymerized onto the castor oil to form the non-ionic surfactant. Suitable PEG hydrogenated castor oils include, PEG 16, 20, 25, 30, 40, 50, 60, 80, 100, and 200. In a preferred embodiment, the non-ionic surfactant is a PEG 40 hydrogenated castor oil commercially available under the trade name Cremophor RH40, a commercially available product from BASF-Wyandotte,

Parsippany, N.J. In certain embodiments, the hydrogenated castor oils used to treat the inorganic compound particulates prior to their incorporation into the dentifrice of the present invention, are prepared by hydrogenating castor oil and treating the hydrogenated product with from about 10 to about 200 moles of ethylene glycol. Ethoxylated hydrogenated castor oil is coated on the silica compounds used in the preparation of the compositions of the present invention at a castor oil to silica weight ratio of about 1:10 to 1:2.

Cationic Active Ingredients

[0034] The present invention provides compositions comprising a cationic active ingredient. As referred to herein, such ingredients include any material comprising a cationic (positively charged) moiety as present in a composition of this invention. In various embodiments, a cationic active ingredient is one, which if in an aqueous composition, would be reactive with an anionic dentifrice component (e.g., silica abrasive). (It should be understood, without limiting the compositions, methods or utility of the present invention, that the reactivity of such cationic active ingredients with an anionic component is reduced or eliminated in the compositions of the present invention.)

[0035] Cationic active ingredients among those useful herein include materials operable to treat or prevent a disorder or provide a cosmetic benefit. In various embodiments, the active is a "systemic active" which is operable to treat or prevent a disorder which, in whole or in part, is not a disorder of the oral cavity. In various embodiments, the active is an "oral care active" operable to treat or prevent a disorder or provide a cosmetic benefit within the oral cavity (e.g., to the teeth, gingival or other hard or soft tissue of the oral cavity). Oral care actives among those useful herein include whitening agents, anticaries agents, tartar control agents,

antiplaque agents, periodontal actives, abrasives, breath freshening agents, malodor control agents, tooth desensitizers, salivary stimulants, and combinations thereof. It is understood that while general attributes of each of the above categories of actives may differ, there may be some common attributes and any given material may serve multiple purposes within two or more of such categories of actives.

[0036] In one embodiment, the cationic active material has an antibacterial or antiattachment benefit. Suitable cationic antibacterial agents for use in oral compositions of the invention include, for example:

(i) quaternary ammonium compounds, such as those in which one or two of the substituents on the quaternary nitrogen has from 8 to 20, preferably from 10 to 18 carbon atoms and is preferably an alkyl group, which may optionally be interrupted by an amide, ester, oxygen, sulfur, or heterocyclic ring, while the remaining substituents have a lower number of carbon atoms, for instance from 1 to 7, and are preferably alkyl, for instance methyl or ethyl, or benzyl. Examples of such compounds include benzalkonium chloride, dodecyl trimethyl ammonium chloride, benzyl dimethyl stearyl ammonium chloride, hexadecyltrimethyl ammonium bromide, benzethonium chloride (diisobutyl p henoxethoxyethyl dimethyl benzyl ammonium chloride) and methyl benzethonium chloride;

(ii) pyridinium and isoquinolinium compounds, including hexadecylpyridinium chloride and alkyl isoquinolinium bromides;

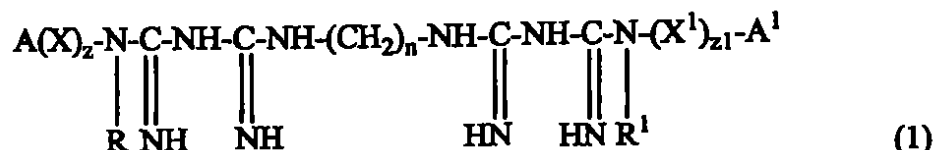
(iii) pyrimidine derivatives such as hexetidine (5-amino-1,3-bis(2-ethylhexyl)-5-methyl-hexahydropyrimidine);

(iv) amidine derivatives such as hexamidine isethionate (4,4'-diamidino- α ω -diphenoxy-hexane isethionate);

v) bispyridine derivatives such as octenidine dihydrochloride (N,N'[1,10-

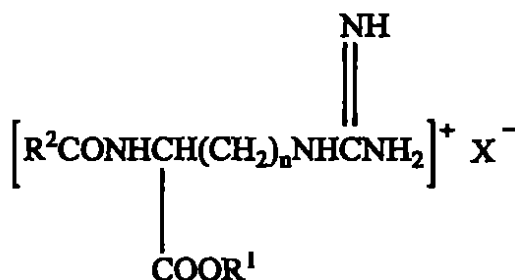
decanediyl-di-1 (4H)-pyridinyl-4-ylidene]-bis (1-octanamine) dihydrochloride);

(vi) guanides, for example, mono-biguanides such as p-chlorobenzyl-biguanide and N'(4-chlorobenzyl)-N''-(2,4-dichlorobenzyl) biguanide, poly(biguanides) such as polyhexamethylene biguanide hydrochloride, and bis-biguanides of the general formula (1):



in which A and A¹ each represent (i) a phenyl group optionally substituted by (C₁₋₄) alkyl, (C₁₋₄) alkoxy, nitro, or halogen, (ii) a (C₁₋₁₂) alkyl group, or (iii) a (C₄₋₁₂) alicyclic group; X and X¹ each represent (C₁₋₃) alkylene; R and R¹ each represent hydrogen, (C₁₋₁₂) alkyl, or aryl (C₁₋₆) alkyl; Z and Z₁ are each 0 or 1; n is an integer from 2 to 12; and the polymethylene chain (CH₂)_n may optionally be interrupted by oxygen or sulfur or an aromatic (for instance phenyl or naphthyl) nucleus; and orally acceptable acid addition salts thereof; examples of such bis-biguanides include chlorhexidine and alexidine. Suitable acid addition salts of the bis-biguanides of general formula (1) include the diacetate, the dihydrochloride and the digluconate. Suitable acid addition salts of chlorhexidine are those which have a water solubility at 20°C of at least 0.005% w/v and include the digluconate, diformate, diacetate, dipropionate, dihydrochloride, dihydroiodide, dilactate, dinitrate, sulphate, and tartrate salts. Preferably the salt is the dihydrochloride, diacetate or digluconate salt of chlorhexidine. Suitable acid addition salts of alexidine include the dihydrofluoride and the dihydrochloride salts; and

vii) N^α-acyl amino acid alkyl esters and salts generally represented by the formula (2) below:



(2)

where R¹ is an alkyl chain of 1 to 8 carbon atoms, preferably from 1 to 3 carbon atoms, and most preferably 3 carbon atoms; R² is an alkyl chain of 6 to 30 carbon atoms, preferably from 10 to 12 carbon atoms, and mixtures thereof; and X is an anion. In various embodiments, the R²CO moiety comprises a natural fatty acid residue such as a natural fatty acid selected from the group consisting of coconut oil fatty acid, tallow fatty acid residue, or a mono-fatty acid residue such as selected from the group consisting of lauroyl (C₁₂), myristyl (C₁₄), stearoyl (C₁₈) fatty acid residues, and mixtures thereof. In one embodiment, the R²CO moiety comprises a lauroyl fatty acid residue.

[0037] X may be any counter-anion that provides a reasonable degree of solubility in water (preferably at least about 1g in 1L of water). Examples of X counter anions which form antibacterial ester salts of the above identified formula, include inorganic acid salts, such as those comprising halogen atoms (e.g., chloride or bromide) or dihydrogen phosphate, or an organic salt such as acetate, taurate, citrate, or pyrrolidone-carboxylate (PCA). The chloride salt is preferred.

[0038] Examples of antibacterial ester compounds preferred in the practice of the present invention are antibacterial ester compound of the above-identified formula wherein n in the formula equals 3 useful in the practice of the present invention include N¹-cocoyl-L-arginine methyl ester, N¹-cocoyl-L-arginine ethyl ester, N¹-cocoyl-L-arginine propyl ester, N¹-stearoyl-L-arginine methyl ester, N¹-

stearoyl-L-arginine ethyl ester hydrochloride. The term 'cocoyl' is an abbreviation for coconut oil fatty acid residue, and chloride salts of these compounds, these ester compounds and the salts thereof being referred to in this specification as arginine derivative compounds. In one embodiment, the arginine derivative compound is the hydrogen chloride salt of ethyl lauroyl arginine.

[0039] Advantageously, the cationic antibacterial agent is present in the range 0.005 to 10 per cent, preferably 0.005 to 5 per cent, more preferably 0.005 to 2.5 per cent by weight of the oral composition.

Oral Care Compositions

[0040] The present invention provides oral care compositions comprising:

- (a) an active ingredient comprising a cationic compound; and
- (b) an inorganic particulate component having a surface substantially coated with a non-ionic surfactant that diminishes chemical interaction between the cationic compound and the inorganic component. Such compositions

preferably comprise an orally-acceptable carrier. In one embodiment, the composition is a dentifrice.

[0041] In various embodiments, the orally-acceptable dentifrice vehicle used to prepare the dentifrice composition comprises a water-phase. The compositions of the present invention optionally include other materials such as adhesion agents, viscosity modifiers, diluents, surfactants, foam modulators, pH modifying agents, humectants, mouth feel agents, sweeteners, flavorants, colorants, and combinations thereof. It is understood that while general attributes of each of the above categories of materials may differ, there may be some common attributes and any given material may serve multiple purposes within two or more of such categories

of materials. Preferably, such carrier materials are selected for compatibility with the cationic active material and other ingredients of the composition.

[0042] The compositions of the present invention preferably comprising a humectant. The humectant is preferably glycerin, sorbitol, xylitol, and/or propylene glycol of molecular weight in the range of 200 to 1,000. Other humectants, such as polyethylene glycol, and mixtures thereof may also be employed. The humectant concentration typically totals about 5 to about 70% by weight of the oral composition.

[0043] Reference hereto to sorbitol refers to the material typically commercially available as a 70% aqueous solution. Water is present typically in amount of at least about 10% by weight, and generally about 15 to 30% by weight of the oral composition. Water employed in the preparation of commercially suitable toothpastes should preferably be deionized and free of organic impurities. These amounts of water include the free water which is added plus that which is introduced with other materials such as with sorbitol.

[0044] Surfactants useful in the practice of the present invention include nonionic, zwitterionic, and anionic surfactants. Suitable nonionic surfactants useful in 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 (e.g., "Tweens", a trademark of ICI US, Inc.). Particularly preferred Polysorbates are Polysorbate 20 (polyoxyethylene 20 sorbitan monolaurate, Tween 20) and Polysorbate 80 (polyoxyethylene 20 sorbitan mono-oleate, Tween 80). Other nontonic surfactants include poly(oxyethylene)-poly(oxypropylene) block copolymers. Such copolymers are known commercially by the non-proprietary name of poloxamers, which name is used in conjunction with a numeric suffix to designate the individual identification of each copolymer.

Poloxamers may have varying contents of ethylene oxide and propylene oxide which results in poloxamers which have a wide range of chemical structures and molecular weights. A preferred poloxamer is Poloxamer 407, sold under the tradename Pluronic F-127 by BASF, Wyandotte, Parsippany, N.J.

[0045] Zwitterion surfactants useful in the practice of the present invention particularly betaine surfactants, include surfactants disclosed in US Patent 5,180,577 incorporated herein by reference. Typical alkyl dimethyl betaines include decyl betaine 2-(N-decyl-N,N-dimethylammonio) acetate, cocobetaine or 2-(N-coc-N, N-dinaethyl ammonio) acetate, myristyl betaine, palmityl betaine, lauryl, betaine, cetyl betaine, cetyl betaine, stearyl betaine, etc. The amido betaines are exemplified by cocoamidoethyl betaine, cocoamidopropyl betaine, laurmidopropyl betaine and the like. The preferred betaine is the cocoainidopropyl betaine.

[0046] In the present invention, non-ionic and zwitterionic surfactants are particularly preferred. However, anionic surfactants, where compatibilized with the cationic active ingredient compounds, may also be useful, and include such surfactants as: water soluble salts of higher fatty acid monoglyceride monosulfates, sodium salts of the monosulfated monoglycerides, or hydrogenated coconut oil fatty acids, higher alkylsulfates, such as sodium lauryl sulfate and alkyl aryl sulfonates, such as sodium dodecyl benzene sulfonate. Other surfactants such as fluorinated surfactants and surface tension reducing materials may also be incorporated within the compositions.

[0047] The surfactant(s) is present in the oral composition of the present invention in the range from about 0.1% to about 5% by weight preferably from about 0.6% to about 2.0% by weight.

[0048] Thickeners used in the compositions of the present invention other than silica thickeners include natural and synthetic gums and colloids. Suitable thickeners include naturally occurring polymers such as carrageenans, xanthan gum, synthetic thickener such as polyglycols of varying molecular weights sold under the tradename Polyox and cellulose polymers such as hydroxyethyl cellulose and hydroxypropyl cellulose. Other inorganic thickeners include natural and synthetic clays such as hectorite clays, lithium magnesium silicate (laponite) and magnesium aluminum silicate (Veegum).

[0049] The thickening agent is present in the dentifrice composition in amounts of about 0.1 to about 10% by weight, preferably about 0.5 to about 4.0% by weight.

[0050] The dentifrice composition of the present invention may also contain a flavoring agent. Flavoring agents which are used in the practice of the present invention include essential oils as well as various flavoring aldehydes, esters, alcohols, and similar materials. Examples of the essential oils include oils of spearmint, peppermint, wintergreen, sassafras, clove, sage, eucalyptus, marjoram, cinnamon, lemon, lime, grapefruit, and orange. Also useful are such chemicals as menthol, carvone, and anethole. Of these, the most commonly employed are the oils of peppermint and spearmint.

[0051] The flavoring agent is incorporated in the dentifrice composition at a concentration of about 0.1 to about 5% by weight and preferably about 0.5 to about 1.5% by weight.

[0052] The compositions of the present invention optionally comprise an additional active material, which is operable for the prevention or treatment of a condition or disorder of hard or soft tissue of the oral cavity, the prevention or

treatment of a physiological disorder or condition, or to provide a cosmetic benefit. In various embodiments, the active is a "systemic active" which is operable to treat or prevent a disorder which, in whole or in part, is not a disorder of the oral cavity. In various embodiments, the active is an "oral care active" operable to treat or prevent a disorder or provide a cosmetic benefit within the oral cavity (e.g., to the teeth, gingival, or other hard or soft tissue of the oral cavity). Oral care actives among those useful herein include whitening agents, anticaries agents, tartar control agents, antiplaque agents, periodontal actives, abrasives, breath freshening agents, malodour control agents, tooth desensitizers, salivary stimulants, and combinations thereof. It is understood that while general attributes of each of the above categories of actives may differ, there may be some common attributes and any given material may serve multiple purposes within two or more of such categories of actives. Preferably, such actives are selected for compatibility with the cationic active material and with other ingredients of the composition. Actives among those useful herein are disclosed in U.S. Patent Publication 2003/0206874, Doyle et al., published November 6, 2003; U.S. Patent 6,290, 933, Durga et al., issued September 18, 2001; and U.S. Patent 6,685,921, Lawlor, issued February 3, 2004.

[0053] In one embodiment, the compositions comprise additional non-cationic antibacterial agents. Such antibacterial agents include those based on phenolic and bisphenolic compounds, such as, halogenated diphenyl ethers, including triclosan (2,4,4'-trichloro-2'-hydroxy-diphenylether, triclocarban (3,4,4-trichlorocarbanilid), as well as 2-phenoxyethanol, benzoate esters, and carbanilides. Such additional antibacterial agents can be present in the oral care composition at quantities of from about 0.01 to about 5% by weight of the oral composition.

[0054] The dentifrice composition of the present invention may also contain a source of fluoride ions or fluorine-providing component, as anticaries agent in amount sufficient to supply about 25 ppm to 5,000 ppm of fluoride ions and include inorganic fluoride salts, such as soluble alkali metal salts. For example, preferred fluoride sources which are compatible with enzymes present in the composition are sodium fluoride, potassium fluoride, sodium fluorosilicate, ammonium fluoro silicate, as well as tin fluorides, such as stannous fluoride and stannous chloride. Sodium fluoride is preferred.

[0055] In addition to fluoride compounds, there may also be included antitartar agents such as zinc salts including zinc chloride, zinc citrate and zinc gluconate which are compatible with the antibacterial ester. These antitartar agents are included in the dentifrice composition at a concentration of about 1 to about 5% by weight.

[0056] Other agents compatible with antibacterial esters also be included in the oral composition of the present invention such as antitartar agents as for example cationic polyphosphates such as water-soluble quaternary aminoalkylene phosphonic compounds as disclosed in US 4,118,472, the disclosure of which is herein incorporated by reference. These antitartar agents may be included in the oral composition of the present invention at a concentration of about 0.1 to about 5% by weight.

[0057] Antitartar agents which are generally recognized as not being compatible with antibacterial esters, such as pyrophosphate and polyphosphate salts, may be included in one component of a dual component oral composition system in which a first component contains the antibacterial ester and the second component contains the incompatible antitartar salt, the first and second components being

maintained separate from each other until dispersed and combined for application to the teeth. Alternatively, such non-compatible antitartar agents may also be included in a single phase dentifrice composition by compatibilization techniques recognized by one of skill in the art, such as providing a low concentration of water to physically separate and prevent diffusion of the non-compatible ingredients thus diminishing contact between them.

[0058] Various other materials may be incorporated in the dentifrice compositions of this invention, including desensitizers, such as potassium nitrate; whitening agents; preservatives; silicones; and chlorophyll compounds. These additives, when present, are incorporated in the dentifrice composition in amounts which do not substantially adversely affect the properties and characteristics desired.

Methods

[0059] In one embodiment, the present invention provides a method of making a dentifrice having an enhanced availability of a cationic oral care active ingredient comprising coating an anionic inorganic component with a non-ionic surfactant to form a cationic-compatible inorganic component. The cationic-compatible inorganic component is added into a dentifrice composition comprising a cationic oral care active compound.

[0060] The preparation of dentifrices is well known in the art. More specifically, to prepare a dentifrice of the present invention, generally the humectants e.g., glycerin, sorbitol, propylene glycol, are dispersed in water in a conventional mixer under agitation. Into the dispersion are added the arginine derivative compound, organic thickeners, such as carageenan, any salts, such as sodium fluoride anticaries agents; and any sweeteners. The resultant mixture is agitated until a

homogeneous gel phase is formed. Into the gel phase are added a pigment such as TiO_2 , and any acid or base required to adjust the pH to 6 to 7. These ingredients are mixed until a homogeneous phase is obtained. The mixture is then transferred to a high speed vacuum mixer; wherein, the surfactant ingredients are added to the mixture as well as the silica compounds such as silica abrasive Zeodent 115 and silica thickener Zeodent 165 both compounds being precoated with an ethoxylated hydrogenated castor oil. The mixture is then mixed at high speed for from 5 to 30 minutes, under vacuum of from about 20 to 50 mm of Hg, preferably about 30 mm Hg. The resultant product is in each case a homogeneous, semi-solid, extrudable paste or gel product.

[0061] The following example further describes and demonstrates preferred embodiments within the scope of the present invention.

Example I

[0062] A toothpaste composition containing ethyl lauroyl arginine HCl (ELAH) and a ethoxylated hydrogenated castor oil precoated coated silica inorganic component and thickener is prepared having the following ingredients:

TABLE I	
Composition (Wt.%)	
Ingredients	A
Polyethylene glycol 600	3
PEG-40 castor oil	6
Hydroxyethylcellulose	1.0
Xanthan	0.2
Sodium saccharin	0.35
Sodium fluoride	0.243
Sorbitol	40
Sodium hydroxide, 50% soln.	0.5
Titanium dioxide	0.5
ELAH	0.5
Zeodent 115	5
Zeodent 165	2
SylodentXWA 650	15
Polysorbate20	1
Cocomidopropyl betaine	1
Flavor	0.72
Water to make	100

[0063] The dentifrice is prepared by dispersing the sorbitol in the water in a conventional mixer under agitation. Into the dispersion is added the xanthan, PEG 40 castor oil, sodium fluoride, hydroxyethyl cellulose, and sodium saccharin. The resultant mixture is agitated until a homogeneous gel phase was formed. Into the gel phase are added TiO_2 and sodium hydroxide to adjust the pH to 6.5. These ingredients are mixed until a homogenous phase was obtained. The mixture is then transferred to a high speed/vacuum mixer; wherein the PEG 40 castor oil coated silica compounds Zeodent 115, Zeodent 165, and Sylodent XWA 650 are added and the

mixture mixed at high speed for 25 minutes, under vacuum from about 30 mm Hg. Finally, polysorbate 20, cocoamidobetaine, flavor and ELAH are added to the mixture and mixed for an additional 10 minutes. The resultant product is a homogeneous, semisolid, extrudable paste or gel product.

[0064] The example and other embodiments described herein are exemplary and not intended to be limiting in describing the full scope of compositions and methods of this invention. Equivalent changes, modifications and variations of specific embodiments, materials, compositions and methods may be made with substantially similar results.

Claims

What is claimed is:

1. A cationic-compatible inorganic component for an oral care composition, said component comprising an anionic particulate substantially coated with a non-ionic surfactant.
2. A cationic-compatible inorganic component according to Claim 1, wherein said non-ionic surfactant comprises an ethoxylated hydrogenated oil.
3. A cationic-compatible inorganic component according to Claim 2, wherein said non-ionic surfactant comprises an ethoxylated hydrogenated hydrocarbon oil having greater than 8 carbon atoms.
4. A cationic-compatible inorganic component according to Claim 3, wherein said ethoxylated hydrogenated hydrocarbon oil comprises ethoxylated hydrogenated castor oil
5. A cationic-compatible inorganic component according to Claim 1, wherein said non-ionic surfactant comprises a hydrophilic moiety comprising one or more polyalkylene oxide compounds.
6. A cationic-compatible inorganic component according to Claim 5, wherein said polyalkylene oxide compound comprises an alkyl group having between 2 to 8 carbon atoms.
7. A cationic-compatible inorganic component according to Claim 6, wherein said polyalkylene oxide comprises polyethylene glycol.
8. A cationic-compatible inorganic component according to Claim 1, wherein said non-ionic surfactant comprises polyoxyethylene (40) hydrogenated castor oil.
9. A cationic-compatible inorganic component according to Claim 1, wherein a

weight ratio of said non-ionic surfactant to said inorganic component is between about 1:10 to about 1:2.

10. An oral care composition according to Claim 9, wherein said inorganic component serves as an abrasive, a thickener, or both in the oral care composition.
11. An oral care composition according to Claim 1, wherein said anionic particulate comprises silica.
12. An oral care composition comprising:
 - (a) an active ingredient comprising a cationic compound; and
 - (b) an inorganic particulate component having a surface substantially coated with a non-ionic surfactant that diminishes chemical interaction between said cationic compound and said inorganic component.
13. An oral care composition according to Claim 12, wherein said cationic compound of said active ingredient is selected from the group of antibacterial compounds consisting of: quaternary ammonium compounds, pyridinium and isoquinolinium compounds, pyrimidine-derivative compounds, pyrimidine derivative compounds, bispyridine derivatives, guanides, N α -acyl amino acid alkyl esters and salts, and mixture thereof.
14. An oral care composition according to Claim 13, wherein said cationic compound of said active ingredient is selected from the group consisting of: benzethonium chloride, octenidine, hexetidine, hexamidine, cetyl pyridinium chloride, chlorhexidine, alexidine, N $^{\alpha}$ -lauroyl-L-arginine ethyl ester hydrochloride mixtures thereof.
15. An oral care composition according to Claim 12, wherein said cationic compound comprises cetyl pyridinium chloride.

16. An oral care composition according to Claim 12, wherein said cationic compound comprises an ethyl lauroyl arginine ester.
17. An oral care composition according to Claim 12, wherein said non-ionic surfactant comprises an ethoxylated hydrogenated oil.
18. An oral care composition according to Claim 17, wherein said ethoxylated hydrogenated hydrocarbon oil comprises ethoxylated hydrogenated castor oil
19. An oral care composition according to Claim 12, wherein said non-ionic surfactant comprises a hydrophilic moiety comprising one or more polyalkylene oxide compounds.
20. An oral care composition according to Claim 20, wherein said polyalkylene oxide comprises polyethylene glycol.
21. An oral care composition according to Claim 20, wherein said non-ionic surfactant comprises polyoxyethylene (40) hydrogenated castor oil.
22. An oral care composition according to Claim 12, wherein said cationic compound is present at a concentration of between about 0.005 to 5 per % by weight of the oral care composition.
23. An oral care composition according to Claim 12, wherein a weight ratio of said non-ionic surfactant to said inorganic component is between about 1:10 to about 1:2.
24. An oral care composition according to Claim 12, wherein said inorganic component comprises silica.
25. An oral care composition according to Claim 12, further comprising one or more dentifrice ingredients selected from the group consisting of: humectant, surfactant, thickening agents, water, fluoride providing agents, antitartar agents, flavor agents, desensitizers, whitening agents, and preservatives.

26. A method of making a dentifrice having an enhanced availability of a cationic oral care active ingredient comprising:

coating an inorganic particulate component with a non-ionic surfactant to form a cationic-compatible inorganic component; and

adding said cationic-compatible inorganic component into a dentifrice composition comprising a cationic oral care active compound.

27. The method according to Claim 26, wherein said inorganic particulate component comprises silica.

28. The method according to Claim 26, wherein said cationic oral care active compound is selected from the group of antibacterial compounds consisting of: quaternary ammonium compounds, pyridinium and isoquinolinium compounds, pyrimidine derivative compounds, pyrimidine derivative compounds, bispyridine derivatives, guanides, N^a-acyl amino acid alkyl esters and salts, and mixture thereof.

29. The method according to Claim 28, wherein said cationic compound comprises an ethyl lauroyl arginine ester.

30. The method according to Claim 28, wherein said cationic compound comprises cetyl pyridinium chloride.

31. The method according to Claim 26, wherein said non-ionic surfactant comprises an ethoxylated hydrogenated oil.

32. The method according to Claim 26, wherein said ethoxylated hydrogenated hydrocarbon oil comprises castor oil

33. The method according to Claim 26, wherein said non-ionic surfactant comprises a hydrophilic moiety comprising one or more polyalkylene oxide compounds.

34. The method according to Claim 33, wherein said polyalkylene oxide comprises polyethylene glycol.
35. The method according to Claim 34, wherein said non-ionic surfactant comprises polyoxyethylene (40) hydrogenated castor oil.
36. The method according to Claim 26, wherein a weight ratio of said non-ionic surfactant to said inorganic component is between about 1:10 to about 1:2.
37. The method according to Claim 26, wherein said dentifrice composition further comprises one or more dentifrice ingredients selected from the group consisting of: humectant, surfactant, thickening agents, water, fluoride providing agents, antitartar agents, flavor agents, desensitizers, whitening agents, and preservatives.

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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)

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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A	US 5 874 068 A (NAIR MONA ET AL) 23 February 1999 (1999-02-23) cited in the application claims 1-14	1-37
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☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

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INTERNATIONAL SEARCH REPORT

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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(54) Título: COMPOSICIONES DENTIFRICAS ESTABLES

(57) Resumen: Un particulado inorgánico compatible con cationes que contiene sílice sustancialmente recubierta con un surfactante no iónico, tal como un aceite de hidrocarburo etoxilado hidrogenado. También se proporcionan composiciones que comprenden un particulado compatible con cationes y un activo catiónico, tal como cloruro de cetil piridinio o un éster de etil lauril arginina.

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**COMPOSICIONES PARA LA HIGIENE ORAL QUE PRESENTAN
PROPIEDADES ANTIPLACA Y REFRESCANTES DEL ALIENTO**

ANTECEDENTES DE LA INVENCION

1. Campo de la Invención

La presente invención se refiere a una composición para la higiene oral que contiene un compuesto éster antibacteriano, la cual composición es efectiva para retardar la acumulación de la placa bacteriana sobre los dientes, y se refiere más particularmente a una composición dentífrica que contiene un compuesto éster antibacteriano que logra una reducción de la placa y con características superiores como refrescadora del aliento.

2. Arte Previo

La halitosis, que es el término técnico para el mal aliento, o *Fetor ex Oris*, es una condición indeseable. De hecho, todo el mundo, con la excepción de las personas muy jóvenes, tiene ocasionalmente mal aliento, habiendo aproximadamente un 25% que lo sufre en una base regular, y el problema tiende a agravarse y a hacerse más frecuente a medida que uno envejece. El problema parece afectar a hombres y mujeres por igual. El mal aliento es el resultado de la descomposición de las proteínas de los alimentos que comemos y de los residuos de la saliva, por las bacterias. Aún la boca más limpia aloja millones de bacterias que tiene la posibilidad de descomponer estas partículas que contienen proteínas, dejadas en la boca. Esta población bacteriana forma productos de

olor desagradable, denominados compuestos azufrados volátiles (CAVs) tales como sulfuro de hidrógeno ("huevos podridos") y mercaptanos metílicos ("olor a zorrino") y otros compuestos olorosos y de sabor desagradable. Hasta el 80 – 90% del mal aliento originado en la boca es debido a este mecanismo.

La placa dental, o bio-película de placa, es una deposición blanda que se forma sobre los dientes y que comprende una acumulación de bacterias y sub-productos tanto salivales como alimenticios. La placa se adhiere tenazmente a los puntos de irregularidad o de discontinuidad, por ejemplo sobre las superficies rugosas de los cálculos, en la línea de las encías, sobre la superficie de la lengua, y dentro de las grietas, y similares. La placa, además de ser antiestética, interviene en la presentación de la gingivitis y de otras formas de enfermedades periodontales.

En el arte ha sido sugerida una amplia variedad de agentes antibacterianos para retardar la formación de las placas y las enfermedades orales y dentales asociadas con la formación de las placas. Por ejemplo, en la Patente de los Estados Unidos No. 5,874,068 y en la UK 1352420 se revela que los compuestos derivados de arginina presentan una actividad antibacteriana cuando son utilizados en composiciones tales como colutorios para contrarrestar la formación de las placas debida a la acumulación bacteriana en la cavidad oral.

Los compuestos derivados de arginina y sus sales en particular muestran un excelente efecto inhibitor contra los microorganismos que poseen una resistencia relativamente elevada contra las bacterias tales como el S.aureus, S. mutans, F. nucleatum, que intervienen en la formación

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de la placa sobre los dientes.

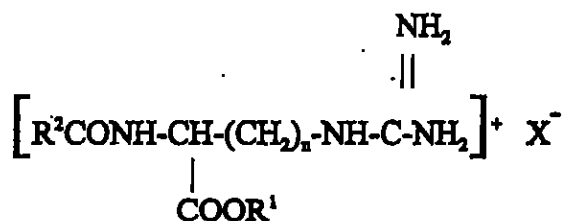
Si bien los compuestos derivados de arginina revelados en el arte previo son agentes antibacterianos efectivos, cuando dichos compuestos son incluidos en dentífricos que contiene sílice, se ha descubierto que cuando el dentífrico era aplicado a los dientes, la biodisponibilidad del compuesto derivado de arginina se reducía a un nivel al cual era poco el beneficio antiplaca obtenido. La investigación de este problema condujo al descubrimiento que los compuestos tales como los abrasivos y espesantes tales como los compuestos silíceos de uso convencional en la preparación de las composiciones dentífricas eran el factor responsable de la reducción de la eficacia antiplaca del compuesto derivado de arginina.

Por lo tanto, en el arte existe una clara necesidad de formular un producto dental capaz de entregar un agente antiplaca - compuesto derivado de arginina mediante el cual los ingredientes utilizados para preparar la composición dentífrica no inhiben la biodisponibilidad del agente antiplaca, de manera tal de lograr máximos beneficios antiplaca.

SÍNTESIS DE LA INVENCION

La presente invención abarca una composición dentífrica que contiene en un vehículo oralmente aceptable una combinación de: (1) un compuesto antibacteriano – derivado de arginina y un compuesto abrasivo, con lo cual una superior reducción de la acumulación de la placa es acompañada por una mayor reducción de los olores desagradables, teniendo el compuesto derivado de arginina la siguiente fórmula:

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en la cual R¹ es una cadena alquilo de 1 a 8 átomos de carbono, R² es una cadena alquilo de 6 a 30 átomos de carbono, y X es un anión; y (2) un compuesto silíceo, habiendo el compuesto silíceo sido primero recubierto con un aceite de castor hidrogenado etoxilado, con lo cual la superior reducción de la acumulación de la placa está acompañada por una mayor reducción de los olores desagradables.

En la práctica de la presente invención, la composición dentífrica que contiene el compuesto antibacteriano de arginina y abrasivos y espesantes silíceos recubiertos con aceite de castor hidroxilado etoxilado, es formulada en forma de una pasta o gel, para lo cual se utiliza un vehículo que contiene una cantidad segura y efectiva del compuesto antibacteriano derivado de arginina, y la presencia del compuesto silíceo no inhibe la biodisponibilidad del compuesto antibacteriano derivado de arginina.

Vehículo del Dentífrico

El vehículo del dentífrico, oralmente aceptable utilizado para preparar la composición dentífrica, comprende una fase acuosa que contiene un humectante en ella. El humectante es preferentemente glicerina, sorbitol, xilitol, y/o propilénglicol con un peso molecular en el intervalo de 200 a 1.000. También pueden emplearse otros humectantes tales como el polietilénglicol, y las mezclas de los mismos. La

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concentración del humectante equivale típicamente de aproximadamente 5 a aproximadamente 70% en peso de la composición total.

La referencia en la presente al sorbitol se refiere al material típicamente obtenible en el comercio en forma de una solución acuosa al 70%. El agua se halla típicamente presente en una cantidad de aproximadamente el 10% en peso, y por lo general de aproximadamente el 15 al 30% en peso de la composición oral. El agua utilizada en la preparación del dentífrico comercialmente adecuado debería ser preferentemente ser agua desionizada y estar exenta de impurezas orgánicas. Dichas cantidades de agua incluyen el agua libre que es adicionada más la que es introducida junto con otros materiales tales como con el sorbitol.

Éster Antibacteriano

En la precedente fórmula de éster antibacteriano, R^2CO puede ser una mezcla de residuos de ácidos grasos en un sistema natural tal como un residuo de ácidos grasos de aceite de coco y ácidos grasos de cebo, y similares, o un residuo de ácidos mono-grasos tales como lauroílo, miristilo, estearoílo, y similares, prefiriéndose el grupo lauroílo.

Los ejemplos de sales de éster antibacterianos de la fórmula anteriormente mencionada incluyen las sales de ácidos inorgánicos tales como el clorhidrato, sulfato, o una sal orgánica tal como acetato, tautarato o citrato, prefiriéndose la sal cloruro.

Los ejemplos de compuestos éster antibacterianos preferidos en la práctica de la presente invención son el compuesto éster antibacteriano de la fórmula anteriormente mencionada en la cual fórmula n es igual a 3, útil

en la práctica de la presente invención, e incluyen el metil éster de N^α-cocoíl-L-arginina, etil éster de N^α-cocoíl-L-arginina, propil éster de N^α-cocoíl-L-arginina, metil éster de N^α estearoíl-L-arginina, clorhidrato de etil éster de N^α estearoíl-L-arginina. La expresión "cocoíl" es una abreviatura de residuo de ácido graso de aceite de coco, y de las sales cloruro de dichos compuestos; en lo que sigue dichos compuestos de éster, y las sales de los mismos, referidos en la presente memoria descriptiva, reciben la designación de compuestos derivados de arginina. La sal del compuesto derivado de arginina, etil lauroíl arginina, es preferida para ser utilizada en la práctica de la presente invención.

El éster antibacteriano de la presente invención se halla presente en las composiciones acuosas orales con una concentración de aproximadamente 0,05 a aproximadamente 2,0 en peso, y preferentemente de aproximadamente 0,075 a aproximadamente 1% en peso.

Compuestos Silíceos

Los abrasivos silíceos útiles en la práctica de la presente invención incluyen los geles de sílice y las sílices amorfas precipitadas. Dichas sílices consisten en partículas coloidales con un tamaño promedio de aproximadamente 3 micrones a aproximadamente 12 micrones, y más preferentemente entre aproximadamente 5 micrones y aproximadamente 10 micrones, con un pH en el intervalo de aproximadamente 4 a 10 y preferentemente de aproximadamente 6 a 9, medido en forma de una suspensión al 5% en peso.

Los abrasivos silíceos ilustrativos útiles en la práctica de la presente invención son comercializados bajo la designación comercial Syldent

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XWA por Davison Chemical Division of W.R. Grace & Co., Baltimore, MD 21203. El Sylodent 650 XWA, es un hidrogel de sílice compuesto de partículas de sílice coloidal que tiene un contenido de agua del 29% en peso, y sus partículas tienen un diámetro promedio de aproximadamente 7 a aproximadamente 10 micrones.

Entre los otros abrasivos utilizados en la práctica de la presente invención se incluyen las sílices precipitadas cuyas partículas tienen un tamaño medio de hasta aproximadamente 20 micrones, tales como el Zeodent 115, comercializado por J.M. Huber Chemicals Division, Havre de Grace, Maryland 21078, o el Sylodent 783 comercializado por Davison Chemical Division of W.R. Grace & Company.

Los materiales silíceos abrasivos pueden ser utilizados individualmente como único abrasivo en la preparación de la composición dental de la presente invención, o en combinación con otros abrasivos dentífricos conocidos tales como el metafosfato de sodio, fosfato dicálcico dihidratado, alúmina calcinada. La cantidad total de abrasivo presente en las composiciones dentífricas de la presente invención se halla en un nivel de aproximadamente 5% a aproximadamente 60% en peso, preferentemente de aproximadamente 10% a aproximadamente 55% en peso cuando la composición dentífrica es una pasta dental.

Los compuestos silíceos que funcionan como agentes espesantes que pueden ser utilizados en la práctica de la presente invención incluyen los compuestos silíceos coloidales disponibles bajo la designación comercial Cab-o-sil manufacturados por Cabot Corporation y distribuidos por Lenape Chemical, Bound Brook, New Jersey; el Zeodent 165 comercializado por

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J.M. Huber Chemicals Division, Havre de Grace, Maryland, 21978; y el Syldent 15, provisto por Davison Chemical Division of W.R. Grace Corporation, Baltimore, Maryland 21203.

Aceite de Castor Hidrogenado Etoxilado

Los aceites de castor hidrogenados etoxilados utilizados para pre-recubrir los compuestos silíceos antes de su incorporación en el dentífrico de la presente invención, son preparados mediante la hidrogenación de aceite de castor y tratando el producto hidrogenado con de aproximadamente 10 a aproximadamente 200 moles de etilénglicol. Estos aceites de castor hidrogenados etoxilados son conocidos por el nombre no propietario de PEG aceites de castor hidrogenados, de acuerdo con el diccionario de Cosmetics, Toiletries and Fragrance Association, Tercera Edición, el cual nombre es utilizado en conjunción con un sufijo numérico para designar el grado de etoxilacion del producto aceite de castor hidrogenado, es decir, la cantidad de moles de óxido de etileno adicionados al producto aceite de castor hidrogenado. Los PEG aceites de castor hidrogenados adecuados incluyen PEG 16, 20, 25, 30, 40, 50, 60, 80, 100 y 200. En una forma de realización preferida, el surfactante PEG 40 aceite de castor hidrogenado es el Cremophor RH40, que es un producto disponible en el comercio provisto por BASF-Wyandotte, Parsipanny, N.J., El aceite de castor hidrogenado etoxilado es aplicado como recubrimiento sobre los compuestos silíceos utilizados en la preparación de las composiciones de la presente invención, con una relación ponderal: aceite de castor/sílice, de aproximadamente 1:10 a 1:2.

Surfactante

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Los surfactantes útiles en la práctica de la presente invención incluyen los surfactantes no-iónicos y los surfactantes zwitteriónicos. Los surfactantes no-iónicos adecuados útiles en la presente invención incluyen los condensados de sorbitano ésteres de ácidos grasos con óxido de etileno (polisorbatos) tales como el monooleato de sorbitano con de aproximadamente 20 a aproximadamente 60 moles de óxido de etileno (por ejemplo, "Tweens", una marca comercial de ICI US, Inc.). Los polisorbatos particularmente preferidos son el Polysorbate 20 (polioxietileno 20 sorbitano monooleato, Tween 20), y el Polysorbate 80 (polioxietileno 20 sorbitano mono-oleato, Tween 80). Entre los otros surfactantes no-iónicos se incluyen los copolímeros de bloque de poli(oxietileno)-poli(oxipropileno). Dichos copolímeros son conocidos comercialmente por el nombre no propietario de poloxámeros, el cual nombre es utilizado en conjunción con un sufijo numérico para designar la identificación individual de cada uno de los copolímeros. Los poloxámeros pueden tener diversos contenidos de óxido de etileno y de óxido de propileno, siendo el resultado poloxámeros que tienen un amplio intervalo de estructuras químicas y de pesos moleculares. Un poloxamero preferido es el Poloxamer 407, vendido bajo la designación comercial Pluronic F-127 por BASF, Wyandotte, Parsipany, N.J.

Los surfactantes zwitteriónicos útiles en la práctica de la presente invención, en particular los surfactantes betaína, incluyen los surfactantes revelados en la Patente de los Estados Unidos No. 5,180,577 incorporada en la presente a título de referencia. Las alquil dimetil betaínas típicas incluyen la decil betaína ó acetato de 2-(N-decil-N,N-dimetilamonio), la

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cocobetaína ó acetato de 2-(N-coc-N,N-dimetil amonio), la miristil betaína, palmitil betaína, lauril betaína, cetil betaína, cetil betaína, estearil betaína, etc. A título de amido betaínas tenemos la cocoamidoetil betaína, cocoamidopropil betaína, laurmidopropil betaína, y similares. La betaína preferida es la cocoamidopropil betaína.

El/los surfactante(s) se hallan presentes en la composición oral de la presente invención en el intervalo de aproximadamente 0,1 a aproximadamente 5% en peso, preferentemente de aproximadamente 0,6% a aproximadamente 2,0 %, en peso.

Agentes Espesantes

Los espesantes utilizados en las composiciones de la presente invención que no son espesantes silíceos, incluyen gomas y coloides naturales y sintéticos. Los espesantes adecuados incluyen los polímeros de presentación natural tales como las carrageninas, goma de xantano, los espesantes sintéticos tales como los poliglicoles de variado peso molecular vendidos bajo la designación comercial Polyox y los polímeros celulósicos tales como la hidroxietil celulosa y la hidroxipropil celulosa. Entre los otros espesantes inorgánicos se incluyen las arcillas naturales y sintéticas tales como las arcillas de hectorita, silicato de líto y magnesio (laponita) y silicato de magnesio y aluminio (Veegum).

El agente espesante se halla presente en la composición dentífrica en cantidades de aproximadamente 0,1 a aproximadamente 10% en peso, preferentemente de aproximadamente 0,5 a aproximadamente 4,0% en peso.

Fluoruro

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La composición dentífrica de la presente invención puede también contener una fuente de iones fluoruro o de componente proveedor de fluor, a título de agente anticaries, en una cantidad suficiente para suministrar aproximadamente 25 ppm a 5.000 ppm de iones fluoruro, e incluyen sales fluoruro inorgánicas tales como sales solubles de metales alcalinos. Por ejemplo, las fuentes de fluoruro preferidas que son compatibles con las enzimas presentes en la composición abarcan el fluoruro de sodio, fluoruro de potasio, fluorsilicato de sodio, fluorsilicato de amonio, como también fluoruros de estaño, tales como el fluoruro estannoso y el cloruro estannoso. Se prefiere el fluoruro de sodio.

Agentes antisarro

Además de los compuestos fluoruro, pueden incluirse agentes antisarro (antitartrato) tales como sales de cinc que incluyen el cloruro de cinc, citrato de cinc y gluconato de cinc que sean compatibles con el éster antibacteriano. Dichos agentes antisarro son incluidos en la composición dentífrica con una concentración de aproximadamente 1 a aproximadamente 5% en peso.

Entre los otros agentes compatibles con los ésteres antibacterianos que también pueden ser incluidos en la composición oral de la presente invención se incluyen los agentes antisarro tales como por ejemplo los polifonatos catiónicos tales como los compuestos cuaternarios aminoalquilenos fosfónicos tales como los revelados en la Patente de los Estados Unidos No. 4,118,472, cuya revelación es incorporada en la presente a título de referencia. Dichos agentes antisarro pueden ser incluidos en la composición oral de la presente invención con una

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concentración de aproximadamente 0,1 a aproximadamente 5% en peso.

Los agentes antisarro que no son compatibles con los ésteres antibacterianos tales como las sales pirofosfato y polifosfato pueden ser incluidos en uno de los componentes de un sistema- composición oral de dos componentes: un primer componente contiene el éster antibacteriano y el segundo componente contiene la sal antisarro incompatible, manteniéndose los componentes primero y segundo separados entre sí hasta ser dispersados y combinados para su aplicación a los dientes.

Sabor

La composición dentífrica de la presente invención también puede contener un agente saborizante. Los agentes saborizantes que son utilizados en la práctica de la presente invención incluyen los aceites esenciales como también diversos aldehídos, ésteres, alcoholes, saborizantes, y materiales similares. Los ejemplos de aceites esenciales incluyen los aceites de menta verde, menta, pirola, safrán, clavel, salvia, eucalipto, mejorana, canela, limón, lima, pomelo, y naranja. También son útiles los productos químicos tales como el mentol, carvona y anetol. Entre los mismos, los más comúnmente utilizados son los aceites de menta y de menta verde.

El agente saborizante es incorporado en la composición dentífrica con una concentración de aproximadamente 0,1 a aproximadamente 5% en peso, y preferentemente de aproximadamente 0,5 a aproximadamente 1,5% en peso.

Otros Ingredientes

Hay varios otros materiales que pueden ser incorporados en la composición dentífrica de la presente invención, e incluyen:

desensibilizantes tales como nitrato de potasio; agentes de blanqueo; agentes preservativos; siliconas; y compuestos de clorofila. Dichos aditivos, caso de hallarse presentes, son incorporados en la composición dentífrica en cantidades que no afecten de manera sustancial las propiedades y características deseadas.

Preparación del Dentífrico

La preparación del dentífrico es bien conocida en el arte. Más específicamente, para preparar un dentífrico de la presente invención, se procede por lo general a dispersar los humectantes por ejemplo la glicerina, sorbitol, propilén glicol, en agua en una mezcladora convencional, bajo agitación. En la dispersión son adicionados el compuesto derivado de arginina, los espesantes orgánicos tales como la carragenina, cualesquiera sales tales como agentes anticaries fluoruro de sodio, y cualesquiera edulcorantes. La mezcla resultante es sometida a agitación hasta que se forma una fase homogénea en forma de un gel. En la fase del gel son adicionados un pigmento tal como el TiO_2 , y cualquier ácido o base requeridos para ajustar el pH a 6 ó 7. Dichos ingredientes son mezclados hasta que se obtiene una fase homogénea. La mezcla es seguidamente transferida a una mezcladora de alta velocidad/vacío en la cual los ingredientes del surfactante son adicionados a la mezcla, como también los compuestos silíceos tales como el abrasivo silíceo Zeodent 115 y el espesante silíceo Zeodent 165, habiendo ambos compuestos sido pre-recubiertos con un aceite de castor hidrogenado etoxilado. La mezcla es seguidamente mezclada a eleva velocidad durante de 5 a 30 minutos, bajo un vacío de aproximadamente 20 a 50 mm de Hg, preferentemente de

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aproximadamente 30 mm de Hg. El producto resultante es en cada caso un producto en forma de pasta o gel, homogéneo, semi-sólido, extruible.

Los siguientes ejemplos sirven para describir mejor aún y demostrar formas de realización preferidas dentro de los alcances de la presente invención. Los ejemplos se dan solamente a título de ilustración, y no han de ser interpretados como una limitación de la presente invención, ya que son posibles muchas variaciones de la misma sin apartarse de su espíritu y alcances.

Ejemplo I

Fueron preparadas composiciones de pasta dental que contenían clorhidrato de etil lauroíl arginina (ELAH) y un agente silíceo abrasivo y espesante recubierto pre-recubierto con aceite de castor hidrogenado etoxilado, en base a los siguientes ingredientes:

TABLA I			
Ingredientes	Composición (% en peso)		
	A	B	C
Polietilenglicol 600	3	3	3
PEG-40 aceite de castor	6	6	0
Hidroxietil celulosa	1,0	1,0	1,0
Xantano	0,2	0,2	0,2
Sacarina sódica	0,35	0,35	0,35
Fluoruro de sodio	0,243	0,243	0,243
Sorbitol	40	40	40
Hidróxido de sodio, sol. al 50%	0,5	0,5	0,5
Dióxido de titanio	0,5	0,5	0,5
ELAH	0,5	0	0,5
Zeodent 115	5	5	5
Zeodent 165	2	2	2
Sylodent XWA 650	15	15	15
Polysorbate 20	1	1	1
Cocomidopropil betaína	1	1	1
Sabor	0,72	0,72	0,72
Agua hasta completar	100	100	100

El dentífrico "Composición A" fue preparado mediante la dispersión del sorbitol en el agua en una mezcladora convencional bajo agitación. En la dispersión fueron adicionados el xantano, PEG 40 aceite de castor, fluoruro de sodio, hidroxietil celulosa, y sacarina de sodio. La mezcla resultante fue sometida a agitación hasta que se formó una fase homogénea de gel. En la fase de gel fue adicionada dióxido de titanio e hidróxido de sodio a efectos de ajustar el pH a 6,5. Estos ingredientes fueron mezclados hasta que se obtuvo una fase homogénea. La mezcla fue seguidamente transferida a una mezcladora de alta velocidad/vacío, en la cual fueron adicionados los compuestos silíceos Zeodent 115, Zeodent 165 y Sylodent XWA 650, recubiertos con PEG aceite de castor, y la mezcla fue sometida a mezclado a alta velocidad durante 25 minutos, bajo un vacío de aproximadamente 30 mm de Hg. Finalmente, el Polysorbate 20, cocoamidobetaína, sabor y ELAH, fueron adicionados a la mezcla y mezclados durante 10 minutos adicionales. El producto resultante era un producto pastoso o en forma de gel, homogéneo, semi-sólido, extruible.

A fines de comparación, se repitió el procedimiento del Ejemplo I para preparar la Composición B, con la salvedad que en la fórmula del dentífrico no se incluyó ELAH. También fue preparada una segunda composición comparativa, la Composición C, en base al procedimiento del Ejemplo, con la salvedad que ni el abrasivo silíceo Zeodent 115 (Composición A) ni el abrasivo silíceo Zeodent 165 (Composición B) presentes en el dentífrico, habían sido recubiertos con el PEG-40 aceite de castor.

La estabilidad del ELAH presente en las composiciones dentífricas

preparadas A, B, C, fue medida mediante titulación con una solución al 0,015% en peso del dentífrico con una solución 0,005N de lauril sulfato de sodio (LSS). Los resultados de la recuperación del ELAH, como indicación de la estabilidad del ELAH, han sido consignados en la siguiente Tabla II.

TABLA II	
Composición	% de recuperación del ELAH
A	87,1
B	3,0
C	7,5
ELAH (placebo)	102,8

La actividad antiplaca de la Composición C fue evaluada mediante un modelo de celda de flujo del tipo revelado en el Journal of Dental Research, vol. 73(II) Págs. 1748-1755 (1994). Se utilizó saliva humana recolectada como fuente de bacterias y prismas simples de cristal de germanio como modelo de superficie oral. Antes de ser expuestas a las bacterias, la superficies fueron tratadas con una suspensión 2:1 de dentífrico / agua, y seguidamente fueron enjuagadas con saliva artificial (1 parte de mucina porcina 25 g/L, y 1 parte de solución tampón de saliva) durante 30 minutos bajo condiciones de caudal de 1 mL / min.

La composición A fue sometida a evaluación para establecer la inhibición general de la placa en comparación con la Composición Comparativa B que no contenía ELAH, y con la Composición C en la cual el abrasivo y espesante silíceos no habían sido pre-recubiertos con PEG-40 aceite de castor. Las composiciones fueron sometidas a ensayo

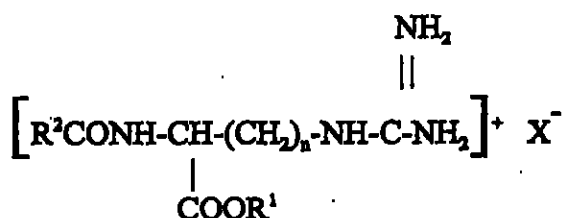
simultáneamente en el sistema. Cuánto más bajo el Puntaje de Placa, tanto más efectivo el agente antiplaca. Los resultados consignados en la siguiente Tabla III muestran una reducción significativa en la placa, lograda mediante la Composición A en comparación con las Composiciones Comparativas B y C.

TABLA III		
Composición	Índice de Placa	% de reducción
A	1,4237	17,5
B	1,7265	—
C	1,6705	3,2

Los resultados consignados en la Tabla III indican que la Composición A que contenía los compuestos silíceos recubiertos con PEG-40 aceite de castor era más efectiva en la reducción de la placa que la Composición C en la cual los compuestos silíceos no habían sido recubiertos con el PEG-40 aceite de castor como también que la Composición B que no contenía ELAH.

REIVINDICACIONES

1. Una composición oral antiplaca estable caracterizada porque comprende un vehículo acuoso que contiene una cantidad segura y efectiva de un compuesto antibacteriano derivado de arginina representado por la fórmula:



en la cual R^1 es una cadena alquilo de 1 a 8 átomos de carbono, R^2 es una cadena alquilo de 6 a 30 átomos de carbono, y X es un anión; y un compuesto de sílice, habiendo el compuesto de sílice sido prereducido con un aceite de castor hidrogenado etoxilado.

2. La composición de acuerdo con la reivindicación 1, caracterizada porque $n = 3$.
3. La composición de acuerdo con la reivindicación 1, caracterizada porque el compuesto derivado de arginina está presente en la composición oral con una concentración de aproximadamente 0,02% a 2% en peso.
4. La composición de acuerdo con la reivindicación 1, caracterizada porque el compuesto antibacteriano derivado de arginina es el clorhidrato de etil lauroil arginina.
5. La composición de acuerdo con la reivindicación 1, caracterizada porque el compuesto de sílice es un abrasivo de sílice.
6. La composición de acuerdo con la reivindicación 1, caracterizada

ST

porque el compuesto de sílice es un espesante de sílice.

7. La composición de acuerdo con la reivindicación 1, **caracterizada** porque el compuesto de sílice ha sido preresubierto con un aceite de castor hidrogenado etoxilado con una relación ponderal entre aceite de castor y sílice, de 1:10 a 1:2.

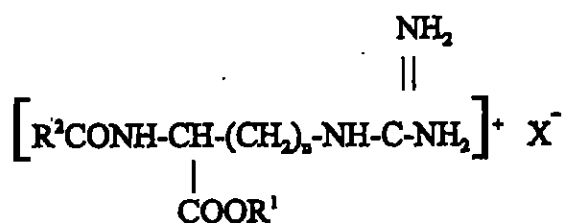
BUENOS AIRES, JUNIO DE 2004.

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RESUMEN

COMPOSICIONES PARA LA HIGIENE ORAL QUE PRESENTAN PROPIEDADES ANTIPLACA Y REFRESCANTES DEL ALIENTO

Una composición oral acuosa antiplaca estable que contiene (a) un compuesto de éster antibacteriano que tiene la fórmula:



en la cual R^1 es una cadena alquilo de 1 a 8 átomos de carbono, y R^2 es una cadena alquilo de 6 a 30 átomos de carbono, y X es un anión; y un compuesto de sílice, prereducido con un aceite de castor hidrogenado etoxilado.

TRANSMITTAL LETTER TO THE UNITED STATES RECEIVING OFFICE

Date	23 June 2004
International Application	
Attorney Docket No.	IR 7345-02

I. Certification under 37 CFR 1.10 (if applicable)

EV 360776381US
Express Mail mailing number

23 June 2004
Date of Deposit

I hereby certify that the application/correspondence attached hereto is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to Assistant Commissioner for Patents, Washington, D.C. 20231.


Signature of person mailing correspondence

Carol Stanley
Typed or printed name of person mailing correspondence

II. ☒ New International Application

TITLE	STABLE DENTIFRICE COMPOSITIONS
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Earliest priority date (Day/Month/Year)
23 June 2003

SCREENING DISCLOSURE INFORMATION: In order to assist in screening the accompanying international application for purposes of determining whether a license for foreign transmittal should and could be granted and for other purposes, the following information is supplied. (Note: check as many boxes as apply):

- A. ☐ The invention disclosed was not made in the United States.
- B. ☐ There is no prior U.S. application relating to this invention.
- C. ☒ The following prior U.S. application(s) contain subject matter which is related to the invention disclosed in the attached international application. (NOTE: priority to these applications may or may not be claimed on form PCT/RO/101 (Request) and this listing does not constitute a claim for priority).

application no.	USSN 10/601,474	filed on	23 June 2003
application no.	USSN To Be Assigned	filed on	23 June 2004

- D. ☐ The present international application ☐ is identical ☐ contains less subject matter than that found in the prior U.S. application(s) identified in paragraph C.
- E. ☐ The present international application ☐ contains additional subject matter not found in the prior U.S. application(s) identified in paragraph C. above. The additional subject matter is found on pages and ☐ DOES NOT ALTER ☐ MIGHT BE CONSIDERED TO ALTER the general nature of the invention in a manner which would require the U.S. application to have been made available for inspection by the appropriate defense agencies under 35 U.S.C. 181 and 37 CFR 5.1. See 37 CFR 5.15

III. ☐ A Response to an Invitation from the RO/US. The following document(s) is (are) enclosed:

- A. ☐ A Request for An Extension of Time to File a Response
- B. ☐ A Power of Attorney (General or Regular)
- C. ☐ Replacement pages:

pages		of the request (PCT/RO/101)	pages		of the figures
pages		of the description	pages		of the abstract
pages		of the claims			

- D. ☐ Submission of Priority Documents

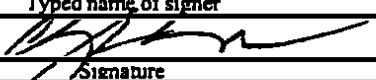
Priority document		Priority document	
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- E. ☐ Fees as specified on attached Fee Calculation sheet form PCT/RO/101 annex

IV. ☐ A Request for Rectification under PCT 91 ☐ A Petition ☐ A Sequence Listing Diskette

V. ☐ Other (please specify):

The person signing this form is the:

☐ Applicant	Clifford E. Wilkins, Jr.
☒ Attorney/Agent (Reg. No.) 39,425	Typed name of signer
☐ Common Representative	
	Signature

512899209EVA3

PCT REQUEST

Original (for SUBMISSION)

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 Prepared Using	PCT-SAFE [EASY mode] Version 3.50 (Build 0002.158)
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	7348-02
I	Title of invention	STABLE DENTIFRICE COMPOSITIONS
II	Applicant	
II-1	This person is:	applicant only
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II-7	State of residence	US
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III-1-6	State of nationality	US
III-1-7	State of residence	US

PCT REQUEST

Original (for SUBMISSION)

64 61

III-2	Applicant and/or inventor	
III-2-1	This person is:	applicant and inventor
III-2-2	Applicant for	US only
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III-2-7	State of residence	US
III-3	Applicant and/or inventor	
III-3-1	This person is:	applicant and inventor
III-3-2	Applicant for	US only
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III-3-6	State of nationality	US
III-3-7	State of residence	US
IV-1	Agent or common representative; or address for correspondence The person identified below is hereby/ has been appointed to act on behalf of the applicant(s) before the competent International Authorities as:	agent
IV-1-1	Name (LAST, First)	PARK, Ellen, K.
IV-1-2	Address:	COLGATE-PALMOLIVE COMPANY 909 River Road Piscataway, New Jersey 08855 United States of America
IV-1-3	Telephone No.	732-878-7157
IV-1-4	Facsimile No.	732-878-7853
IV-1-5	e-mail	ellen_park@colpal.com
IV-1-6	Agent's registration No.	34055
IV-2	Additional agent(s)	additional agent(s) with same address as first named agent
IV-2-1	Name(s)	WILKINS, Clifford, E., Jr. (39,425)
V	DESIGNATIONS	
V-1	The filing of this request constitutes under Rule 4.9(a), the designation of all Contracting States bound by the PCT on the international filing date, for the grant of every kind of protection available and, where applicable, for the grant of both regional and national patents.	

PCT REQUEST

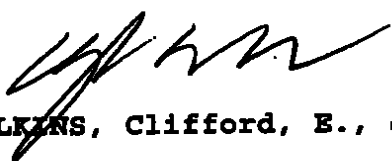
Original (for SUBMISSION)

VI-1	Priority claim of earlier national application		
VI-1-1	Filing date	23 June 2003 (23.06.2003)	
VI-1-2	Number	10/601,474	
VI-1-3	Country	US	
VI-2	Priority claim of earlier national application		
VI-2-1	Filing date	23 June 2004 (23.06.2004)	
VI-2-2	Number		
VI-2-3	Country	US	
VI-3	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, VI-2	
VII-1	International Searching Authority Chosen	European Patent Office (EPO) (ISA/EP)	
VIII	Declarations	Number of declarations	
VIII-1	Declaration as to the identity of the inventor	-	
VIII-2	Declaration as to the applicant's entitlement, as at the international filing date, to apply for and be granted a patent	-	
VIII-3	Declaration as to the applicant's entitlement, as at the international filing date, to claim the priority of the earlier application	-	
VIII-4	Declaration of inventorship (only for the purposes of the designation of the United States of America)	-	
VIII-5	Declaration as to non-prejudicial disclosures or exceptions to lack of novelty	-	
IX	Check list	number of sheets	electronic file(s) attached
IX-1	Request (including declaration sheets)	4	✓
IX-2	Description	25	-
IX-3	Claims	5	-
IX-4	Abstract	1	✓
IX-5	Drawings	0	-
IX-7	TOTAL	35	
	Accompanying items	paper document(s) attached	electronic file(s) attached
IX-8	Fee calculation sheet	✓	-
IX-17	PCT-SAFE physical media	-	✓
IX-19	Figure of the drawings which should accompany the abstract		
IX-20	Language of filing of the international application	English	

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PCT REQUEST

Original (for SUBMISSION)

X-1	Signature of applicant, agent or common representative	
X-1-1	Name (LAST, First)	WILKINS, Clifford, E., Jr.
X-1-2	Name of signatory	
X-1-3	Capacity	

FOR RECEIVING OFFICE USE ONLY

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	

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

BACKGROUND

[0001] The present invention relates to an oral care composition which contains an inorganic particulate component in an oral care composition, and more particularly to a dentifrice composition containing a cationic-compatible inorganic particulate component with an oral care active antibacterial compound, which achieves plaque reduction with superior breath freshening characteristics.

[0002] Halitosis, the technical term for bad breath, or *Fetor ex Oris*, is an undesirable condition. As a matter of fact, everyone, excluding the very young, occasionally has bad breath, with approximately 25% suffering on a regular basis and the problem tends to get worse and more frequent as one gets older. The problem seems to be evenly split between men and women. Bad breath results when proteins from the food we eat and saliva debris are broken down by bacteria. Even the cleanest mouth hosts millions of bacteria which have the potential to decompose these protein-containing particles left in the mouth. This bacterial population forms foul smelling products, called volatile sulfur compounds (VSC) - such as hydrogen sulfide ("rotten eggs") and methyl mercaptans ("skunk smell") and other odorous and bad tasting compounds. Up to 80-90% of bad breath that originates in the mouth is by this mechanism.

[0003] Dental plaque or plaque bio-film is a soft deposit that forms on teeth and is comprised of an accumulation of bacteria and salivary as well as food by-products. Plaque adheres tenaciously at the points of irregularity or discontinuity, e.g., on rough calculus surfaces, at the gum line, on tongue surface and within crevices, and the like. Besides being unsightly, plaque is implicated in the occurrence of gingivitis and other forms of periodontal disease.

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[0004] A wide variety of antibacterial agents have been suggested in the art to retard plaque formation and the oral infections and dental disease associated with plaque formation. For example US 5,874,068 and GB 1352420 disclose that arginine derivative compounds exhibit antibacterial activity when used in oral compositions such as mouthrinses to counter plaque formation by bacterial accumulation in the oral cavity. Arginine derivative compounds and their salts in particular show excellent inhibitory effect against microorganisms which possess relatively strong resistance to bacterial such as *S. aureus*, *S. mutans*, *F. nucleatum* which are involved in plaque formation on teeth. Other cationic oral care active ingredients, such as bis biguanides or cetyl pyridinium chloride (CPC) are also known for their inhibitory effect on plaque formation and bacterial accumulation in the oral cavity.

[0005] Although the cationic active material compounds, such as for example, the arginine derivative compounds disclosed in the prior art, are effective antibacterial agents, when these compounds are included in silica containing dentifrice it was discovered that when the dentifrice was applied to the teeth, the bioavailability of the arginine derivative compound was reduced to a level whereby little antiplaque benefit was achieved. Investigation of this problem led to the discovery that compounds such as abrasives and thickeners such as silica compounds conventionally used in the preparation of dentifrice compositions were the factor responsible for the impairment of the antiplaque efficacy of the arginine derivative compound.

[0006] Thus, there is a clear need in the art to formulate a dental product capable of delivering a cationic active antiplaque antibacterial agent whereby the

ingredients used to prepare the dentifrice composition do not inhibit the bioavailability of the cationic antiplaque agent so that optimum antiplaque benefits result.

SUMMARY

[0007] In one aspect, the present invention provides a cationic-compatible inorganic component for an oral care composition comprising an inorganic particulate component comprising silica and having a surface substantially coated with a non-ionic surfactant to form the cationic-compatible inorganic component.

[0008] In another aspect the present invention provides an oral care composition comprising an active ingredient comprising a cationic compound and an inorganic particulate component having a surface substantially coated with a non-ionic surfactant.

[0009] In yet another aspect, the present invention provides a method of making a dentifrice having an enhanced availability of a cationic oral care active ingredient comprising coating an inorganic particulate component with a non-ionic surfactant to form a cationic-compatible inorganic component, and adding the cationic-compatible inorganic component into a dentifrice composition comprising a cationic oral care active compound.

[0010] It has been discovered that compositions and methods of this invention afford advantages over prior art oral care compositions using cationic antibacterial ingredients and inorganic particulates, such as those known in the art. Such advantages over the art include one or more of the following: enhanced bioavailability and efficacy of a cationic active ingredient translating to improved antibacterial and/or antiplaque efficacy, potential to reduce concentrations of cationic active materials in oral care compositions comprising an inorganic particulate, potential expansion of the active ingredients useful in dentifrice oral compositions.

Further uses, benefits and embodiments of the present invention are apparent from the description set forth herein.

DESCRIPTION

[0011] The following definitions and non-limiting guidelines must be considered in reviewing the description of this invention set forth herein. The headings (such as "Introduction" and "Summary,") and sub-headings (such as, "Cationic Active Ingredients", "Inorganic Particulate Components", "Non-Ionic Surfactant" "Additional Antimicrobial Active Ingredients", "Dentifrice Vehicle", "Surfactants" "Thickening Agents", "Flavor Agents", "Fluoride Providing Agents", "Antitartar Agents", "Other Ingredients", and "Methods") used herein are intended only for general organization of topics within the disclosure of the invention, and are not intended to limit the disclosure of the invention or any aspect thereof. In particular, subject matter disclosed in the "Introduction" may include aspects of technology within the scope of the invention, and may not constitute a recitation of prior art. Subject matter disclosed in the "Summary" is not an exhaustive or complete disclosure of the entire scope of the invention or any embodiments thereof. Classification or discussion of a material within a section of this specification as having a particular utility is made for convenience, and no inference should be drawn that the material must necessarily or solely function in accordance with its classification herein when it is used in any given composition.

[0012] The citation of any references herein does not constitute an admission that those references are prior art or have any relevance to the patentability of the invention disclosed herein. Any discussion of the content of references cited in the Introduction is intended merely to provide a general summary of assertions made by the authors of the references, and does not constitute an admission as to the

accuracy of the content of such references. All references cited in the Description section of this specification are hereby incorporated by reference in their entirety.

[0013] The description and any specific examples, while indicating embodiments of the invention, are intended for purposes of illustration only and are not intended to limit the scope of the invention. Moreover, recitation of multiple embodiments having stated features is not intended to exclude other embodiments having additional features, or other embodiments incorporating different combinations the stated of features. Specific Examples are provided for illustrative purposes of how to make and use the compositions and methods of this invention and, unless explicitly stated otherwise, are not intended to be a representation that given embodiments of this invention have, or have not, been made or tested.

[0014] As used herein, the words "preferred" and "preferably" refer to embodiments of the invention that afford certain benefits, under certain circumstances. However, other embodiments may also be preferred, under the same or other circumstances. Furthermore, the recitation of one or more preferred embodiments does not imply that other embodiments are not useful, and is not intended to exclude other embodiments from the scope of the invention.

[0015] As used herein, the word "include," and its variants, is intended to be non-limiting, such that recitation of items in a list is not to the exclusion of other like items that may also be useful in the materials, compositions, devices, and methods of this invention.

[0016] As referred to herein, all compositional percentages are by weight of the total composition, unless otherwise specified.

[0017] As referred to herein, the word "substantially," when applied to a characteristic of a composition or method of this invention, indicates that there may

be variation in the characteristic without having substantial effect on the chemical or physical attributes of the composition or method.

[0018] As used herein, the term "about," when applied to the value for a parameter of a composition or method of this invention, indicates that the calculation or the measurement of the value allows some slight imprecision without having a substantial effect on the chemical or physical attributes of the composition or method. If, for some reason, the imprecision provided by "about" is not otherwise understood in the art with this ordinary meaning, then "about" as used herein indicates a possible variation of up to 5% in the value.

Inorganic Particulate Components

[0019] The present invention provides cationic-compatible inorganic components for an oral care composition, said components comprising an anionic particulate substantially coated with a non-ionic surfactant. Without limiting the compositions, methods or utility of the present invention, in various embodiments, the inorganic particulate components afford diminished interaction between cationic active compounds (discussed below) and silica relative to the interaction between such materials that would occur in a prior art aqueous composition, thus optimizing the bioavailability of the cationic active compounds.

[0020] Anionic particulates among those useful herein include silica, alumina, or both. In one embodiment, the inorganic component material comprises silica. Silica abrasives useful in the practice of the present invention include silica gels and precipitated amorphous silicas. These silicas are colloidal particles/particulates having an average particle size ranging from about 3 microns to about 12 microns, and more preferably between about 5 to about 10 microns and a pH range from 4 to 10 preferably 6 to 9 when measured as a 5% by weight slurry.

[0021] Illustrative of silica abrasives useful in the practice of the present invention are marketed under the trade designation Sylodent XWA by Davison Chemical Division of W.R. Grace & Co., Baltimore, MD 21203. Sylodent 650 XWA, a silica hydrogel composed of particulates of colloidal silica having a water content of 29% by weight averaging from about 7 to about 10 microns in diameter.

[0022] Other inorganic component abrasives used in the practice of the present invention include precipitated silicas having a mean particle size of up to about 20 microns, such as Zeodent 115, marketed by J.M. Huber Chemicals Division, Havre de Grace, Maryland 21078, or Sylodent 783 marketed by Davison Chemical Division of W.R. Grace & Company.

[0023] The silica abrasive materials may be used individually as the sole abrasive in preparing the dental composition of the present invention or in combination with other known dentifrice abrasives such as sodium metaphosphate, dihydrated dicalcium phosphate, calcined alumina. The total quantity of abrasive present in the dentifrice compositions of the present invention is at a level of from about 5% to about 60% by weight, preferably from about 10% to about 55% by weight when the dentifrice composition is a toothpaste.

[0024] Silica compounds which function as thickening agents which may be used in the practice of the present invention include colloidal silica compounds available under the trade designation Cabo-sil 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; and Sylodent 15, available from Davison Chemical Division of W.R. Grace Corporation, Baltimore, Maryland.

Non-Ionic Surfactant

[0025] In one aspect of the current invention, inorganic particulates that are otherwise incompatible with cationic antimicrobial agents are rendered compatible with the agents by treatment or reaction with a nonionic surfactant prior to their formulation in dentifrice compositions along with the cationic material. The improved compatibility is shown for example, from *in vitro* measurements of availability of the various antimicrobial agents of the compositions of the invention.

[0026] Although the invention is not to be limited by any theory of action of the non-ionic surfactant, it is believed that the reaction or treatment of the inorganic particulates with the nonionic surfactant results in the deposition or attachment of nonionic surfactant molecules to the inorganic particulates, which results in a coating of substantially all of the charged surface of the inorganic particulates. Still not to be limited by theory, the deposition or attachment may be by either physical means, chemical means, or a combination thereof. Thus, the nonionic surfactant molecules may be held or deposited on the surface of the inorganic particulates by van der Waals attractions, hydrogen bonds, the formation of covalent bonds with reactive species on the surface of the particulates, and so on. The inorganic particulates of the present invention generally have a negative charge, and are thus considered to be anionic.

[0027] On a molecular level, surface active agents (or surfactants) are understood as being made of two moieties. The first is a hydrophilic moiety and the second is a hydrophobic moiety. As is well known, surfactants "work" by interacting with one phase of material at its surface. The resulting structure mediates the interfacial interaction of the phase with other phases. An important consideration in the action of surface active agents is the relative strength of the respective hydrophilic and hydrophobic portions of the molecule. The relative strength can be expressed and

understood as a balance between the hydrophilic characteristics of one part of the molecule and the hydrophobic characteristics of another.

[0028] Nonionic surfactants are made of chemical constituents that result in a molecule having no ionic charges. As such, the nonionic surfactant are distinguished from cationic surfactants, anionic surfactants, and amphoteric surfactants. In a preferred embodiment, the hydrophilic moiety of a nonionic surfactant is based on a polyoxyalkylene structure. A polyoxyalkylene structure is a polyether type polymer that formally represents the polymerization product of a wide variety of cyclic ethers that polymerize by ring opening polymerization. Non-ionic surfactants useful in the invention are usually synthesized by the polymerization of such cyclic ethers.

[0029] Among the cyclic ethers that may be polymerized to form the hydrophilic portion of the nonionic surfactant of the invention are those having from two to eight carbon atoms, with ring structures of three to five atoms. Suitable cyclic ether systems for polymerization include oxiranes (three membered rings), oxetanes (four member rings), and furans (five-membered rings). The surfactants may be made by homo or copolymerization of one or more of such cyclic ethers. In a preferred embodiment, oxiranes are polymerized under basic catalysis, followed by neutralization of the polymeric product. Polyoxyalkylene or polyether hydrophilic moieties may also be produced by acid catalyzed polymerization of cyclic ethers.

[0030] The size and relative proportion of alkylene groups in the polyoxyalkylene hydrophilic moiety determines its relative hydrophilic nature. In general the hydrophilic nature is related to the proportion of lower cyclic ethers that are present in the polymerization mix. In a preferred embodiment, the polyoxyalkylene hydrophilic moiety of the surfactant is made of polyoxyethylene,

resulting from the polymerization of ethylene oxide. (Ethylene oxide is an oxirane containing two carbons). Relatively smaller amounts of propyleneoxide, butyleneoxide, and other higher cyclic ethers may be copolymerized with the ethylene oxide to form the hydrophilic moieties on the surfactant of the invention, as long as the balance of hydrophilic and hydrophobic character in the resulting surfactant is suitable for application in the invention.

[0031] The hydrophobic moieties on the non ionic surfactants of the invention are generally organic radicals containing at least about twelve carbons. These surfactants are made by polymerizing ethylene oxide or a mixture of alkylene oxides and/or cyclic ethers onto an organic molecule that serves as a starting material. The starting material contains at least about 12 carbon atoms, and an organic group containing an active hydrogen that will react with the cyclic ethers to form the polyoxyalkylene. Reactive organic groups containing active hydrogen include without limitation, hydroxyl, carboxyl, amine, amide, and mercaptan. A preferred reactive group is hydroxyl, whereby the starting material is an organic alcohol containing at least about 12 carbon atoms. Thus, suitable nonionic surfactants may be prepared by polymerizing ethylene oxide or a mixture of cyclic ethers onto fatty alcohols, fatty acids, fatty acid amides, and the like. Commercially available fatty alcohols, fatty acids, fatty amides and fatty amines includes those containing from about 12 to about 26 carbon atoms.

[0032] In a preferred embodiment, the hydrophobic moiety is based on hydroxyl functional diglycerides and triglycerides. Such diglycerides and triglycerides are available as vegetable oils. In a preferred embodiment, castor oil, a triglyceride containing hydroxyl functionality is used to make the nonionic surfactants of the invention. In a preferred embodiment, ethyleneoxide or a mixture of cyclic

ethers is polymerized onto castor oil until at least about 10, preferably about 20, and more preferably about 40 alkylene oxide units are added per molecule of the oil. Preferably, the extent of alkoxylation is less than 600, preferably less than 400, and more preferably less than 200. The castor oil alkoxyate resulting from the polymerization may then be hydrogenated by conventional means to form a hydrogenated castor oil alkoxyate. Alternatively, the castor oil, which in its native form contains olefinic unsaturation, may be hydrogenated prior to the reaction of the hydroxyl functional oil with the cyclic ethers. Thus, in a preferred embodiment, the nonionic surfactant comprises a castor oil alkoxyate or a hydrogenated alkoxyate having from about 20 to 200 repeating oxyalkylene units in the hydrophilic moiety. In a preferred embodiment, the oxyalkylene units are predominantly oxyethylene. In a particularly preferred embodiment, the polyoxyalkylene moiety is polyoxyethylene.

[0033] Ethoxylated castor oil and hydrogenated ethoxylated castor oils are known by the non-proprietary name of PEG hydrogenated castor oils, in accordance with dictionary of the Cosmetics, Toiletries and Fragrance Association, 3rd Edition which name is used in conjunction with a numeric suffix to designate the degree of ethoxylation of the hydrogenated castor oil product, i.e., the number of moles of ethylene oxide added to the hydrogenated castor oil product. Such ethoxylated and hydrogenated ethoxylated castor oils are commercially available and are commonly designated as PEG NN castor oil or PEG NN hydrogenated castor oil, where NN designates the number of ethylene oxide units polymerized onto the castor oil to form the non-ionic surfactant. Suitable PEG hydrogenated castor oils include, PEG 16, 20, 25, 30, 40, 50, 60, 80, 100, and 200. In a preferred embodiment, the non-ionic surfactant is a PEG 40 hydrogenated castor oil commercially available under the trade name Cremophor RH40, a commercially available product from BASF-Wyandotte,

Parsippany, N.J. In certain embodiments, the hydrogenated castor oils used to treat the inorganic compound particulates prior to their incorporation into the dentifrice of the present invention, are prepared by hydrogenating castor oil and treating the hydrogenated product with from about 10 to about 200 moles of ethylene glycol. Ethoxylated hydrogenated castor oil is coated on the silica compounds used in the preparation of the compositions of the present invention at a castor oil to silica weight ratio of about 1:10 to 1:2.

Cationic Active Ingredients

[0034] The present invention provides compositions comprising a cationic active ingredient. As referred to herein, such ingredients include any material comprising a cationic (positively charged) moiety as present in a composition of this invention. In various embodiments, a cationic active ingredient is one, which if in an aqueous composition, would be reactive with an anionic dentifrice component (e.g., silica abrasive). (It should be understood, without limiting the compositions, methods or utility of the present invention, that the reactivity of such cationic active ingredients with an anionic component is reduced or eliminated in the compositions of the present invention.)

[0035] Cationic active ingredients among those useful herein include materials operable to treat or prevent a disorder or provide a cosmetic benefit. In various embodiments, the active is a "systemic active" which is operable to treat or prevent a disorder which, in whole or in part, is not a disorder of the oral cavity. In various embodiments, the active is an "oral care active" operable to treat or prevent a disorder or provide a cosmetic benefit within the oral cavity (e.g., to the teeth, gingival or other hard or soft tissue of the oral cavity). Oral care actives among those useful herein include whitening agents, anticaries agents, tartar control agents,

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antiplaque agents, periodontal actives, abrasives, breath freshening agents, malodor control agents, tooth desensitizers, salivary stimulants, and combinations thereof. It is understood that while general attributes of each of the above categories of actives may differ, there may be some common attributes and any given material may serve multiple purposes within two or more of such categories of actives.

[0036] In one embodiment, the cationic active material has an antibacterial or antiattachment benefit. Suitable cationic antibacterial agents for use in oral compositions of the invention include, for example:

(i) quaternary ammonium compounds, such as those in which one or two of the substituents on the quaternary nitrogen has from 8 to 20, preferably from 10 to 18 carbon atoms and is preferably an alkyl group, which may optionally be interrupted by an amide, ester, oxygen, sulfur, or heterocyclic ring, while the remaining substituents have a lower number of carbon atoms, for instance from 1 to 7, and are preferably alkyl, for instance methyl or ethyl, or benzyl. Examples of such compounds include benzalkonium chloride, dodecyl trimethyl ammonium chloride, benzyl dimethyl stearyl ammonium chloride, hexadecyltrimethyl ammonium bromide, benzethonium chloride (diisobutyl p henoxethoxyethyl dimethyl benzyl ammonium chloride) and methyl benzethonium chloride;

(ii) pyridinium and isoquinolinium compounds, including hexadecylpyridinium chloride and alkyl isoquinolinium bromides;

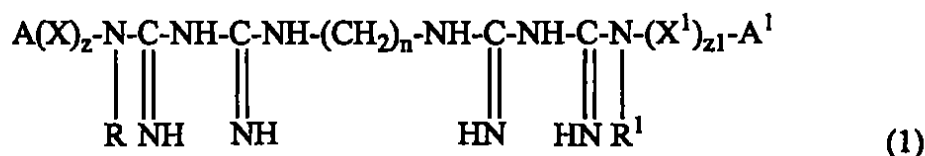
(iii) pyrimidine derivatives such as hexetidine (5-amino-1,3-bis(2-ethylhexyl)-5-methyl-hexahydropyrimidine);

(iv) amidine derivatives such as hexamidine isethionate (4,4'-diamidino- α ω -diphenoxy-hexane isethionate);

v) bispyridine derivatives such as octenidine dihydrochloride (N,N'[1,10-

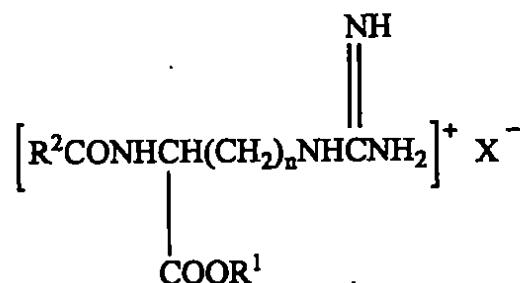
decanediyldi-1 (4H)-pyridinyl-4-ylidene]-bis (1-octanamine) dihydrochloride);

(vi) guanides, for example, mono-biguanides such as p-chlorobenzyl-biguanide and N'(4-chlorobenzyl)-N''-(2,4-dichlorobenzyl) biguanide, poly(biguanides) such as polyhexamethylene biguanide hydrochloride, and bis-biguanides of the general formula (1):



in which A and A¹ each represent (i) a phenyl group optionally substituted by (C₁₋₄) alkyl, (C₁₋₄) alkoxy, nitro, or halogen, (ii) a (C₁₋₁₂) alkyl group, or (iii) a (C₄₋₁₂) alicyclic group; X and X¹ each represent (C₁₋₃) alkylene; R and R¹ each represent hydrogen, (C₁₋₁₂) alkyl, or aryl (C₁₋₆) alkyl; Z and Z₁ are each 0 or 1; n is an integer from 2 to 12; and the polymethylene chain (CH₂)_n may optionally be interrupted by oxygen or sulfur or an aromatic (for instance phenyl or naphthyl) nucleus; and orally acceptable acid addition salts thereof; examples of such bis-biguanides include chlorhexidine and alexidine. Suitable acid addition salts of the bis-biguanides of general formula (1) include the diacetate, the dihydrochloride and the digluconate. Suitable acid addition salts of chlorhexidine are those which have a water solubility at 20°C of at least 0.005% w/v and include the digluconate, diformate, diacetate, dipropionate, dihydrochloride, dihydroiodide, dilactate, dinitrate, sulphate, and tartrate salts. Preferably the salt is the dihydrochloride, diacetate or digluconate salt of chlorhexidine. Suitable acid addition salts of alexidine include the dihydrofluoride and the dihydrochloride salts; and

vii) N^α-acyl amino acid alkyl esters and salts generally represented by the formula (2) below:



(2)

where R¹ is an alkyl chain of 1 to 8 carbon atoms, preferably from 1 to 3 carbon atoms, and most preferably 3 carbon atoms; R² is an alkyl chain of 6 to 30 carbon atoms, preferably from 10 to 12 carbon atoms, and mixtures thereof; and X is an anion. In various embodiments, the R²CO moiety comprises a natural fatty acid residue such as a natural fatty acid selected from the group consisting of coconut oil fatty acid, tallow fatty acid residue, or a mono-fatty acid residue such as selected from the group consisting of lauroyl (C₁₂), myristyl (C₁₄), stearoyl (C₁₈) fatty acid residues, and mixtures thereof. In one embodiment, the R²CO moiety comprises a lauroyl fatty acid residue.

[0037] X may be any counter-anion that provides a reasonable degree of solubility in water (preferably at least about 1g in 1L of water). Examples of X counter anions which form antibacterial ester salts of the above identified formula, include inorganic acid salts, such as those comprising halogen atoms (e.g., chloride or bromide) or dihydrogen phosphate, or an organic salt such as acetate, taurate, citrate, or pyrrolidone-carboxylate (PCA). The chloride salt is preferred.

[0038] Examples of antibacterial ester compounds preferred in the practice of the present invention are antibacterial ester compound of the above-identified formula wherein n in the formula equals 3 useful in the practice of the present invention include N¹-cocoyl-L-arginine methyl ester, N^α-cocoyl-L-arginine ethyl ester, N^α-cocoyl-L-arginine propyl ester, N^α-stearoyl-L-arginine methyl ester, N^α-

stearoyl-L-arginine ethyl ester hydrochloride. The term 'cocoyl' is an abbreviation for coconut oil fatty acid residue, and chloride salts of these compounds, these ester compounds and the salts thereof being referred to in this specification as arginine derivative compounds. In one embodiment, the arginine derivative compound is the hydrogen chloride salt of ethyl lauroyl arginine.

[0039] Advantageously, the cationic antibacterial agent is present in the range 0.005 to 10 per cent, preferably 0.005 to 5 per cent, more preferably 0.005 to 2.5 per cent by weight of the oral composition.

Oral Care Compositions

[0040] The present invention provides oral care compositions comprising:

- (a) an active ingredient comprising a cationic compound; and
- (b) an inorganic particulate component having a surface substantially coated with a non-ionic surfactant that diminishes chemical interaction between the cationic compound and the inorganic component. Such compositions

preferably comprise an orally-acceptable carrier. In one embodiment, the composition is a dentifrice.

[0041] In various embodiments, the orally-acceptable dentifrice vehicle used to prepare the dentifrice composition comprises a water-phase. The compositions of the present invention optionally include other materials such as adhesion agents, viscosity modifiers, diluents, surfactants, foam modulators, pH modifying agents, humectants, mouth feel agents, sweeteners, flavorants, colorants, and combinations thereof. It is understood that while general attributes of each of the above categories of materials may differ, there may be some common attributes and any given material may serve multiple purposes within two or more of such categories

of materials. Preferably, such carrier materials are selected for compatibility with the cationic active material and other ingredients of the composition.

[0042] The compositions of the present invention preferably comprising a humectant. The humectant is preferably glycerin, sorbitol, xylitol, and/or propylene glycol of molecular weight in the range of 200 to 1,000. Other humectants, such as polyethylene glycol, and mixtures thereof may also be employed. The humectant concentration typically totals about 5 to about 70% by weight of the oral composition.

[0043] Reference hereto to sorbitol refers to the material typically commercially available as a 70% aqueous solution. Water is present typically in amount of at least about 10% by weight, and generally about 15 to 30% by weight of the oral composition. Water employed in the preparation of commercially suitable toothpastes should preferably be deionized and free of organic impurities. These amounts of water include the free water which is added plus that which is introduced with other materials such as with sorbitol.

[0044] Surfactants useful in the practice of the present invention include nonionic, zwitterionic, and anionic surfactants. Suitable nonionic surfactants useful in 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 (e.g., "Tweens", a trademark of ICI US, Inc.). Particularly preferred Polysorbates are Polysorbate 20 (polyoxyethylene 20 sorbitan monolaurate, Tween 20) and Polysorbate 80 (polyoxyethylene 20 sorbitan mono-oleate, Tween 80). Other nontonic surfactants include poly(oxyethylene)-poly(oxypropylene) block copolymers. Such copolymers are known commercially by the non-proprietary name of poloxamers, which name is used in conjunction with a numeric suffix to designate the individual identification of each copolymer.

Poloxamers may have varying contents of ethylene oxide and propylene oxide which results in poloxamers which have a wide range of chemical structures and molecular weights. A preferred poloxamer is Poloxamer 407, sold under the tradename Pluronic F-127 by BASF, Wyandotte, Parsippany, N.J.

[0045] Zwitterion surfactants useful in the practice of the present invention particularly betaine surfactants, include surfactants disclosed in US Patent 5,180,577 incorporated herein by reference. Typical alkyl dimethyl betaines include decyl betaine 2-(N-decyl-N,N-dimethylammonio) acetate, cocobetaine or 2-(N-coc-N, N-dimethyl ammonio) acetate, myristyl betaine, palmityl betaine, lauryl betaine, cetyl betaine, cetyl betaine, stearyl betaine, etc. The amido betaines are exemplified by cocoamidoethyl betaine, cocoamidopropyl betaine, lauramidopropyl betaine and the like. The preferred betaine is the cocoamidopropyl betaine.

[0046] In the present invention, non-ionic and zwitterionic surfactants are particularly preferred. However, anionic surfactants, where compatibilized with the cationic active ingredient compounds, may also be useful, and include such surfactants as: water soluble salts of higher fatty acid monoglyceride monosulfates, sodium salts of the monosulfated monoglycerides, or hydrogenated coconut oil fatty acids, higher alkylsulfates, such as sodium lauryl sulfate and alkyl aryl sulfonates, such as sodium dodecyl benzene sulfonate. Other surfactants such as fluorinated surfactants and surface tension reducing materials may also be incorporated within the compositions.

[0047] The surfactant(s) is present in the oral composition of the present invention in the range from about 0.1% to about 5% by weight preferably from about 0.6% to about 2.0% by weight.

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[0048] Thickeners used in the compositions of the present invention other than silica thickeners include natural and synthetic gums and colloids. Suitable thickeners include naturally occurring polymers such as carrageenans, xanthan gum, synthetic thickener such as polyglycols of varying molecular weights sold under the tradename Polyox and cellulose polymers such as hydroxyethyl cellulose and hydroxypropyl cellulose. Other inorganic thickeners include natural and synthetic clays such as hectorite clays, lithium magnesium silicate (laponite) and magnesium aluminum silicate (Veegum).

[0049] The thickening agent is present in the dentifrice composition in amounts of about 0.1 to about 10% by weight, preferably about 0.5 to about 4.0% by weight.

[0050] The dentifrice composition of the present invention may also contain a flavoring agent. Flavoring agents which are used in the practice of the present invention include essential oils as well as various flavoring aldehydes, esters, alcohols, and similar materials. Examples of the essential oils include oils of spearmint, peppermint, wintergreen, sassafras, clove, sage, eucalyptus, marjoram, cinnamon, lemon, lime, grapefruit, and orange. Also useful are such chemicals as menthol, carvone, and anethole. Of these, the most commonly employed are the oils of peppermint and spearmint.

[0051] The flavoring agent is incorporated in the dentifrice composition at a concentration of about 0.1 to about 5% by weight and preferably about 0.5 to about 1.5% by weight.

[0052] The compositions of the present invention optionally comprise an additional active material, which is operable for the prevention or treatment of a condition or disorder of hard or soft tissue of the oral cavity, the prevention or

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treatment of a physiological disorder or condition, or to provide a cosmetic benefit. In various embodiments, the active is a "systemic active" which is operable to treat or prevent a disorder which, in whole or in part, is not a disorder of the oral cavity. In various embodiments, the active is an "oral care active" operable to treat or prevent a disorder or provide a cosmetic benefit within the oral cavity (e.g., to the teeth, gingival, or other hard or soft tissue of the oral cavity). Oral care actives among those useful herein include whitening agents, anticaries agents, tartar control agents, antiplaque agents, periodontal actives, abrasives, breath freshening agents, malodour control agents, tooth desensitizers, salivary stimulants, and combinations thereof. It is understood that while general attributes of each of the above categories of actives may differ, there may be some common attributes and any given material may serve multiple purposes within two or more of such categories of actives. Preferably, such actives are selected for compatibility with the cationic active material and with other ingredients of the composition. Actives among those useful herein are disclosed in U.S. Patent Publication 2003/0206874, Doyle et al., published November 6, 2003; U.S. Patent 6,290, 933, Durga et al., issued September 18, 2001; and U.S. Patent 6,685,921, Lawlor, issued February 3, 2004.

[0053] In one embodiment, the compositions comprise additional non-cationic antibacterial agents. Such antibacterial agents include those based on phenolic and bisphenolic compounds, such as, halogenated diphenyl ethers, including triclosan (2,4,4'-trichloro-2'-hydroxy-diphenylether, triclocarban (3,4,4-trichlorocarbanilid), as well as 2-phenoxyethanol, benzoate esters, and carbanilides. Such additional antibacterial agents can be present in the oral care composition at quantities of from about 0.01 to about 5% by weight of the oral composition.

[0054] The dentifrice composition of the present invention may also contain a source of fluoride ions or fluorine-providing component, as anticaries agent in amount sufficient to supply about 25 ppm to 5,000 ppm of fluoride ions and include inorganic fluoride salts, such as soluble alkali metal salts. For example, preferred fluoride sources which are compatible with enzymes present in the composition are sodium fluoride, potassium fluoride, sodium fluorosilicate, ammonium fluoro silicate, as well as tin fluorides, such as stannous fluoride and stannous chloride. Sodium fluoride is preferred.

[0055] In addition to fluoride compounds, there may also be included antitartar agents such as zinc salts including zinc chloride, zinc citrate and zinc gluconate which are compatible with the antibacterial ester. These antitartar agents are included in the dentifrice composition at a concentration of about 1 to about 5% by weight.

[0056] Other agents compatible with antibacterial esters also be included in the oral composition of the present invention such as antitartar agents as for example cationic polyphosphates such as water soluble quaternary aminoalkylene phosphonic compounds as disclosed in US 4,118,472, the disclosure of which is herein incorporated by reference. These antitartar agents may be included in the oral composition of the present invention at a concentration of about 0.1 to about 5% by weight.

[0057] Antitartar agents which are generally recognized as not being compatible with antibacterial esters, such as pyrophosphate and polyphosphate salts, may be included in one component of a dual component oral composition system in which a first component contains the antibacterial ester and the second component contains the incompatible antitartar salt, the first and second components being

maintained separate from each other until dispersed and combined for application to the teeth. Alternatively, such non-compatible antitartar agents may also be included in a single phase dentifrice composition by compatibilization techniques recognized by one of skill in the art, such as providing a low concentration of water to physically separate and prevent diffusion of the non-compatible ingredients thus diminishing contact between them.

[0058] Various other materials may be incorporated in the dentifrice compositions of this invention, including desensitizers, such as potassium nitrate; whitening agents; preservatives; silicones; and chlorophyll compounds. These additives, when present, are incorporated in the dentifrice composition in amounts which do not substantially adversely affect the properties and characteristics desired.

Methods

[0059] In one embodiment, the present invention provides a method of making a dentifrice having an enhanced availability of a cationic oral care active ingredient comprising coating an anionic inorganic component with a non-ionic surfactant to form a cationic-compatible inorganic component. The cationic-compatible inorganic component is added into a dentifrice composition comprising a cationic oral care active compound.

[0060] The preparation of dentifrices is well known in the art. More specifically, to prepare a dentifrice of the present invention, generally the humectants e.g., glycerin, sorbitol, propylene glycol, are dispersed in water in a conventional mixer under agitation. Into the dispersion are added the arginine derivative compound, organic thickeners, such as carageenan, any salts, such as sodium fluoride anticaries agents; and any sweeteners. The resultant mixture is agitated until a

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homogeneous gel phase is formed. Into the gel phase are added a pigment such as TiO_2 , and any acid or base required to adjust the pH to 6 to 7. These ingredients are mixed until a homogeneous phase is obtained. The mixture is then transferred to a high speed vacuum mixer; wherein, the surfactant ingredients are added to the mixture as well as the silica compounds such as silica abrasive Zeodent 115 and silica thickener Zeodent 165 both compounds being precoated with an ethoxylated hydrogenated castor oil. The mixture is then mixed at high speed for from 5 to 30 minutes, under vacuum of from about 20 to 50 mm of Hg, preferably about 30 mm Hg. The resultant product is in each case a homogeneous, semi-solid, extrudable paste or gel product.

[0061] The following example further describes and demonstrates preferred embodiments within the scope of the present invention.

Example I

[0062] A toothpaste composition containing ethyl lauroyl arginine HCl (ELAH) and a ethoxylated hydrogenated castor oil precoated coated silica inorganic component and thickener is prepared having the following ingredients:

TABLE I	
Composition (Wt.%)	
Ingredients	A
Polyethylene glycol 600	3
PEG-40 castor oil	6
Hydroxyethylcellulose	1.0
Xanthan	0.2
Sodium saccharin	0.35
Sodium fluoride	0.243
Sorbitol	40
Sodium hydroxide, 50% soln.	0.5
Titanium dioxide	0.5
ELAH	0.5
Zeodent 115	5
Zeodent 165	2
SylodentXWA 650	15
Polysorbate20	1
Cocomidopropyl betaine	1
Flavor	0.72
Water to make	100

[0063] The dentifrice is prepared by dispersing the sorbitol in the water in a conventional mixer under agitation. Into the dispersion is added the xanthan, PEG 40 castor oil, sodium fluoride, hydroxyethyl cellulose, and sodium saccharin. The resultant mixture is agitated until a homogeneous gel phase was formed. Into the gel phase are added TiO_2 and sodium hydroxide to adjust the pH to 6.5. These ingredients are mixed until a homogenous phase was obtained. The mixture is then transferred to a high speed/vacuum mixer; wherein the PEG 40 castor oil coated silica compounds Zeodent 115, Zeodent 165, and Sylodent XWA 650 are added and the

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mixture mixed at high speed for 25 minutes, under vacuum from about 30 mm Hg.

Finally, polysorbate 20, cocoamidobetaine, flavor and ELAH are added to the mixture and mixed for an additional 10 minutes. The resultant product is a homogeneous, semisolid, extrudable paste or gel product.

[0064] The example and other embodiments described herein are exemplary and not intended to be limiting in describing the full scope of compositions and methods of this invention. Equivalent changes, modifications and variations of specific embodiments, materials, compositions and methods may be made with substantially similar results.

What is claimed is:

1. A cationic-compatible inorganic component for an oral care composition, said component comprising an anionic particulate substantially coated with a non-ionic surfactant.
2. A cationic-compatible inorganic component according to Claim 1, wherein said non-ionic surfactant comprises an ethoxylated hydrogenated oil.
3. A cationic-compatible inorganic component according to Claim 2, wherein said non-ionic surfactant comprises an ethoxylated hydrogenated hydrocarbon oil having greater than 8 carbon atoms.
4. A cationic-compatible inorganic component according to Claim 3, wherein said ethoxylated hydrogenated hydrocarbon oil comprises ethoxylated hydrogenated castor oil
5. A cationic-compatible inorganic component according to Claim 1, wherein said non-ionic surfactant comprises a hydrophilic moiety comprising one or more polyalkylene oxide compounds.
6. A cationic-compatible inorganic component according to Claim 5, wherein said polyalkylene oxide compound comprises an alkyl group having between 2 to 8 carbon atoms.
7. A cationic-compatible inorganic component according to Claim 6, wherein said polyalkylene oxide comprises polyethylene glycol.
8. A cationic-compatible inorganic component according to Claim 1, wherein said non-ionic surfactant comprises polyoxyethylene (40) hydrogenated castor oil.
9. A cationic-compatible inorganic component according to Claim 1, wherein a

weight ratio of said non-ionic surfactant to said inorganic component is between about 1:10 to about 1:2.

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10. An oral care composition according to Claim 9, wherein said inorganic component serves as an abrasive, a thickener, or both in the oral care composition.
 11. An oral care composition according to Claim 1, wherein said anionic particulate comprises silica.
 12. An oral care composition comprising:
 - (a) an active ingredient comprising a cationic compound; and
 - (b) an inorganic particulate component having a surface substantially coated with a non-ionic surfactant that diminishes chemical interaction between said cationic compound and said inorganic component.
 13. An oral care composition according to Claim 12, wherein said cationic compound of said active ingredient is selected from the group of antibacterial compounds consisting of: quaternary ammonium compounds, pyridinium and isoquinolinium compounds, pyrimidine derivative compounds, pyrimidine derivative compounds, bispyridine derivatives, guanides, Na-acyl amino acid alkyl esters and salts, and mixture thereof.
 14. An oral care composition according to Claim 13, wherein said cationic compound of said active ingredient is selected from the group consisting of: benzethonium chloride, octenidine, hexetidine, hexamidine, cetyl pyridinium chloride, chlorhexidine, alexidine, N^a-lauroyl-L-arginine ethyl ester hydrochloride mixtures thereof.
 15. An oral care composition according to Claim 12, wherein said cationic compound comprises cetyl pyridinium chloride.

16. An oral care composition according to Claim 12, wherein said ~~cationic~~ compound comprises an ethyl lauroyl arginine ester. 91
17. An oral care composition according to Claim 12, wherein said non-ionic surfactant comprises an ethoxylated hydrogenated oil.
18. An oral care composition according to Claim 17, wherein said ethoxylated hydrogenated hydrocarbon oil comprises ethoxylated hydrogenated castor oil
19. An oral care composition according to Claim 12, wherein said non-ionic surfactant comprises a hydrophilic moiety comprising one or more polyalkylene oxide compounds.
20. An oral care composition according to Claim 20, wherein said polyalkylene oxide comprises polyethylene glycol.
21. An oral care composition according to Claim 20, wherein said non-ionic surfactant comprises polyoxyethylene (40) hydrogenated castor oil.
22. An oral care composition according to Claim 12, wherein said cationic compound is present at a concentration of between about 0.005 to 5 per % by weight of the oral care composition.
23. An oral care composition according to Claim 12, wherein a weight ratio of said non-ionic surfactant to said inorganic component is between about 1:10 to about 1:2.
24. An oral care composition according to Claim 12, wherein said inorganic component comprises silica.
25. An oral care composition according to Claim 12, further comprising one or more dentifrice ingredients selected from the group consisting of: humectant, surfactant, thickening agents, water, fluoride providing agents, antitartar agents, flavor agents, desensitizers, whitening agents, and preservatives.

26. A method of making a dentifrice having an enhanced availability of a cationic oral care active ingredient comprising:

coating an inorganic particulate component with a non-ionic surfactant to form a cationic-compatible inorganic component; and

adding said cationic-compatible inorganic component into a dentifrice composition comprising a cationic oral care active compound.

27. The method according to Claim 26, wherein said inorganic particulate component comprises silica.

28. The method according to Claim 26, wherein said cationic oral care active compound is selected from the group of antibacterial compounds consisting of: quaternary ammonium compounds, pyridinium and isoquinolinium compounds, pyrimidine derivative compounds, pyrimidine derivative compounds, bispyridine derivatives, guanides, N^α-acyl amino acid alkyl esters and salts, and mixture thereof.

29. The method according to Claim 28, wherein said cationic compound comprises an ethyl lauroyl arginine ester.

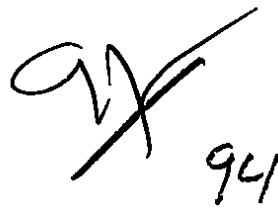
30. The method according to Claim 28, wherein said cationic compound comprises cetyl pyridinium chloride.

31. The method according to Claim 26, wherein said non-ionic surfactant comprises an ethoxylated hydrogenated oil.

32. The method according to Claim 26, wherein said ethoxylated hydrogenated hydrocarbon oil comprises castor oil

33. The method according to Claim 26, wherein said non-ionic surfactant comprises a hydrophilic moiety comprising one or more polyalkylene oxide compounds.

34. The method according to Claim 33, wherein said polyalkylene oxide comprises polyethylene glycol.
35. The method according to Claim 34, wherein said non-ionic surfactant comprises polyoxyethylene (40) hydrogenated castor oil.
36. The method according to Claim 26, wherein a weight ratio of said non-ionic surfactant to said inorganic component is between about 1:10 to about 1:2.
37. The method according to Claim 26, wherein said dentifrice composition further comprises one or more dentifrice ingredients selected from the group consisting of: humectant, surfactant, thickening agents, water, fluoride providing agents, antitartar agents, flavor agents, desensitizers, whitening agents, and preservatives.



STABLE DENTIFRICE COMPOSITIONS

Abstract

A cationic-compatible inorganic particulate comprising silica substantially coated with a non-ionic surfactant, such as an ethoxylated hydrogenated hydrocarbon oil. Compositions comprising the cationic-compatible particulate and a cationic active, such as cetyl pyridinium chloride or an ethyl lauryl arginine ester, are also provided.

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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.)

Bernard Lieberman, Rosemary M. Miano, Ellen K. Park and Clifford E. Wilkins, Jr. of

COLGATE-PALMOLIVE COMPANY

909 River Road.

P.O. Box 1343

Piscataway, New Jersey 08855-1343

United States of America

to represent the undersigned before



all the competent International Authorities



the International Searching Authority only



the International Preliminary Examining Authority only

in connection with any and all international applications filed by the undersigned with the following Office

RO/US

as receiving Office

and to make or receive payments on behalf of the undersigned.

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):

COLGATE-PALMOLIVE COMPANY

By

Andrew D. Hendry

Senior Vice President, General Counsel and Secretary

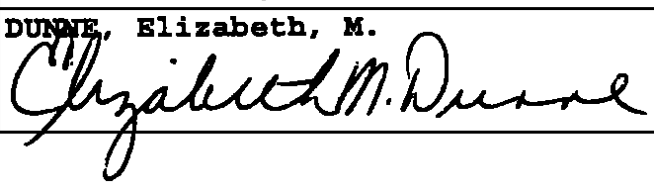
Date: April 8, 2004

29 96

PCT (ANNEX - FEE CALCULATION SHEET)

Original (for SUBMISSION)

(This sheet is not part of and does not count as a sheet of the international application)

0	For receiving Office use only			
0-1	International Application No.			
0-2	Date stamp of the receiving Office			
0-4	Form PCT/RO/101 (Annex) PCT Fee Calculation Sheet			
0-4-1	Prepared Using	PCT-SAFE [EASY mode] Version 3.50 (Build 0002.158)		
0-8	Applicant's or agent's file reference	7348-02		
2	Applicant	COLGATE-PALMOLIVE COMPANY		
12	Calculation of prescribed fees	fee amount/multiplier	Total amounts (USD)	
12-1	Transmittal fee T	⇒	300	
12-2-1	Search fee S	⇒	1818	
12-2-2	International search to be carried out by	EP		
12-3	International filing fee (first 30 sheets) H	1035		
12-4	Remaining sheets	5		
12-5	Additional amount (X)	11		
12-6	Total additional amount I2	55		
12-7	H + I2 = I	1090		
12-12	EASY Filing reduction R	-74		
12-13	Total international filing fee (I-R) I	⇒	1016	
12-14	Fee for priority document Number of priority documents requested	2		
12-15	Fee per document (X)	20		
12-16	Total priority document fee: P	⇒	40	
12-17	TOTAL FEES PAYABLE (T+S+I+P)	⇒	3174	
12-18	Mode of payment	authorization to charge deposit account		
12-20	Deposit account instructions The receiving Office	United States Patent and Trademark Office (USPTO) (RO/US)		
12-20-1	Authorization to charge the total fees indicated above.	✓		
12-20-2	Authorization to charge any deficiency or credit any overpayment in the total fees indicated above.	✓		
12-20-3	Authorization to charge the fee for priority document.	✓		
12-21	Deposit account No.	03-2457		
12-22	Date	23 June 2004 (23.06.2004)		
12-23	Name and signature	DUNNE, Elizabeth, M. 		

PATENT COOPERATION TREATY

PCT

From the INTERNATIONAL SEARCHING AUTHORITY

To:

COLGATE PALMOLIVE COMPANY
Attn. Park, Ellen K.
909 River Road
Piscataway, NJ 08855
UNITED STATES OF AMERICA

DEC - 2 2004

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT AND
THE WRITTEN OPINION OF THE INTERNATIONAL
SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

Date of mailing
(day/month/year)

30/11/2004

Applicant's or agent's file reference

7348-02

10/601-474

FOR FURTHER ACTION

See paragraphs 1 and 4 below

International application No.

PCT/US2004/020033

International filing date
(day/month/year)

23/06/2004

Applicant

COLGATE-PALMOLIVE COMPANY

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO, 34 chemin des Colombettes
1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

- ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. Reminders

Shortly after the expiration of 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within 19 months from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later); otherwise, the applicant must, within 20 months from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of 30 months (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the International Searching Authority

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

Authorized officer

Marthe Oldendorf

10/1

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These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the letter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

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The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 48.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

PATENT COOPERATION TREATY
PCT

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INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 7348-02	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/US2004/020033	International filing date (day/month/year) 23/06/2004	(Earliest) Priority Date (day/month/year) 23/06/2003
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 4 sheets.

☒ 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, see Box No. I.

2. ☐ Certain claims were found unsearchable (See Box II).

3. ☐ Unity of invention is lacking (see Box III).

4. With regard to the title,

☒ 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,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regards to the drawings,

a. the figure of the drawings to be published with the abstract is Figure No. _____

☐ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

b. ☐ none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US2004/020038

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A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K7/00

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)

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4 837 008 A (RUDY JEROME B ET AL) 6 June 1989 (1989-06-06) column 3, line 37 - line 54 column 5, line 68	1-37
A	US 5 874 068 A (NAIR MONA ET AL) 23 February 1999 (1999-02-23) cited in the application claims 1-14	1-37
A	EP 0 422 803 A (BEECHAM GROUP PLC) 17 April 1991 (1991-04-17) page 4, line 34 - page 5, line 16; claims 1-17	1-37
A	US 4 110 083 A (BENEDICT JAMES JOHN) 29 August 1978 (1978-08-29) claims 1-7	1-37
	-/--	

☒ 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.

G document member of the same patent family

Date of the actual completion of the international search

17 November 2004

Date of mailing of the international search report

30/11/2004

Name and mailing address of the ISA

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

Authorized officer

Richards, M

INTERNATIONAL SEARCH REPORT

International Application No. **PCT/US2004/020033** **102**

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 3 151 027 A (BROGE ROBERT W ET AL) 29 September 1964 (1964-09-29) claims 1-11 -----	1-37

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US2004/020033

Patent document cited in search report		Publication date	Patent family member(s)	Publication date	103
US 4837008	A	06-06-1989	US CA US	4971782 A 1286994 C 4897258 A	20-11-1990 30-07-1991 30-01-1990
US 5874068	A	23-02-1999	AU WO ZA	1379999 A 9929289 A1 9811182 A	28-06-1999 17-06-1999 08-06-1999
EP 0422803	A	17-04-1991	AU AU CA EP IE JP NO NZ PT ZA	644104 B2 6360890 A 2026509 A1 0422803 A2 903492 A1 3127718 A 904252 A 235498 A 95463 A 9007781 A	02-12-1993 18-04-1991 12-04-1991 17-04-1991 24-04-1991 30-05-1991 12-04-1991 26-05-1993 25-06-1991 27-05-1992
US 4110083	A	29-08-1978	CA DE FR GB IT JP JP JP US	1063357 A1 2522046 A1 2271840 A1 1506045 A 1036898 B 1291110 C 51032743 A 60009484 B 4157387 A	02-10-1979 04-12-1975 19-12-1975 05-04-1978 30-10-1979 29-11-1985 19-03-1976 11-03-1985 05-06-1979
US 3151027	A	29-09-1964	NONE		

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PCT

see form PCT/ISA/220

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**
(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

FOR FURTHER ACTION
See paragraph 2 below

Priority date (day/month/year)
23.06.2003

International Patent Classification (IPC) or both national classification and IPC
A61K7/00

Applicant
COLGATE-PALMOLIVE COMPANY

- 1. This opinion contains indications relating to the following items:**

- | | |
|--|---|
| ☒ Box No. I | Basis of the opinion |
| ☒ Box No. II | Priority |
| ☐ Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| ☐ Box No. IV | Lack of unity of invention |
| ☒ Box No. V | Reasoned statement under Rule 43bis.1 (a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| ☐ Box No. VI | Certain documents cited |
| ☐ Box No. VII | Certain defects in the international application |
| ☐ Box No. VIII | Certain observations on the international application |

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1 *bis(b)* that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/SA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office - P.B. 5818 Patentaan 2
NL-2280 HV Rijswijk - Pays Bas
Tel. +31 70 340 - 2040 Tx: 31 651 epo nl
Fax: +31 70 340 - 3016

Authorized Officer

Richards, M

Telephone No. +31 70 340-4267



**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2004/020033

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Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2004/020033

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Box No. II Priority

1. ☒ The following document has not been furnished:

☒ copy of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(a)).

☐ translation of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43bis.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-37
	No: Claims	
Inventive step (IS)	Yes: Claims	1-37
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-37
	No: Claims	

2. Citations and explanations

see separate sheet

Item V

The following documents are referred to in this communication:

- D1 : US 4 837 008 A (RUDY JEROME B ET AL) 6 June 1989 (1989-06-06)
- D2 : US 5 874 068 A (NAIR MONA ET AL) 23 February 1999 (1999-02-23)
- D3 : EP 0 422 803 A (BEECHAM GROUP PLC) 17 April 1991 (1991-04-17)
- D4 : US 4 110 083 A (BENEDICT JAMES JOHN) 29 August 1978 (1978-08-29)
- D5 : US 3 151 027 A (BROGE ROBERT W ET AL) 29 September 1964 (1964-09-29)

Novelty (Article 33(2) PCT)

None of D1 - D5 disclose a component according to claim 1 wherein said component comprises an anionic particulate substantially coated with a non-ionic surfactant. It follows that there is also no disclosure of the oral care composition comprising said component according to claim 12, or of a method of making a dentifrice comprising said component according to claim 26. The subject matter of the dependent claims is also not disclosed.

Thus claims 1 - 37 are acknowledged as novel.

Inventivity (Article 33(3) PCT)

The present application addresses the problem of improving bioavailability of the cationic antiplaque agent in dentifrice compositions such that optimum antiplaque benefits result. The solution to said problem is the coating of anionic particulates with a non-ionic surfactant according to present claim 1.

D1 discloses a dentifrice composition comprising abrasives which may be coated with a water-soluble barrier coating, see column 3 line 41 - line 53. Suitable coatings include polyethylene glycol, see column 5 line 68. However D1 does not suggest using nonionic surfactants as coatings, furthermore D1 does not suggest improving the bioavailability of antiplaque agents by coating the abrasives with nonionic coatings.

Inventivity of the present set of claims is thus acknowledged.

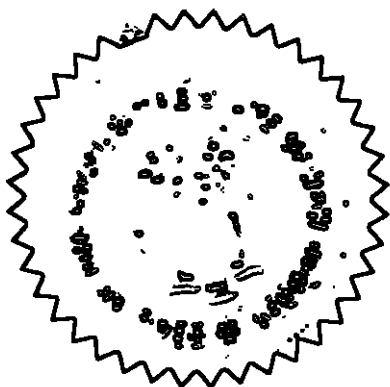
APOSTILLE

(CONVENTION DE LA HAYE DU 5 OCTOBRE 1961)

1. COUNTRY: UNITED STATES OF AMERICA
2. THIS PUBLIC DOCUMENT HAS BEEN SIGNED BY:
ELAINE M FLYNN
3. ACTING IN THE CAPACITY OF:
COUNTY CLERK
4. BEARS THE SEAL/STAMP OF:
COUNTY OF MIDDLESEX

CERTIFIED

5. AT TRENTON, NEW JERSEY
6. THE 9TH DAY OF NOVEMBER 2005
7. BY: John E McCormac, CPA, NEW JERSEY TREASURER
8. NO. A243562
9. SEAL/STAMP:
10. SIGNATURE



A handwritten signature in dark ink, appearing to read "John E. McCormac". The signature is written in a cursive style with a horizontal line extending to the right.

STATE OF NEW JERSEY }
County of Middlesex } ss

I ELAINE M FLYNN Clerk of the County of Middlesex do hereby certify that

CAROL M STANLEY

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whose name is subscribed to the annexed certificate or proof of acknowledgment of the annexed instrument was at the time of taking the same a

NOTARY PUBLIC OF NEW JERSEY

acting in and for said county duly commissioned and sworn and qualified to act as such that as such

NOTARY PUBLIC OF NEW JERSEY

he was duly authorized by the laws of the State of New Jersey to take and certify depositions to administer oaths and affirmations to take affidavits and certify the acknowledgment and proof of deeds and other written instruments for lands tenements and hereditaments to be read in evidence or recorded in this state and further that I am well acquainted with the handwriting of such

NOTARY PUBLIC OF NEW JERSEY

and verify that the signature to such proof or acknowledgment is genuine

IN TESTIMONY WHEREOF I have hereunto set my hand and affixed the seal of the County of Middlesex this 4 day of NOV. 20 05

Elaine M Flynn CLERK



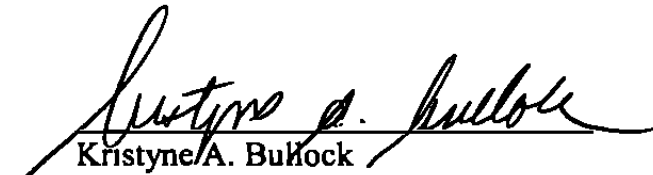
111

COUNTY OF MIDDLESEX

STATE OF NEW JERSEY

UNITED STATES OF AMERICA

I, Kristyne A. Bullock, of COLGATE-PALMOLIVE COMPANY, do hereby declare that the copies attached hereto are true photocopies of the assignments in support of U.S. Serial No. 10/601,474 filed June 23, 2003 and U.S. Serial No. 10/875,063 filed June 23, 2004.


Kristyne A. Bullock
Patent Attorney

Subscribed and sworn to
before me this 30 day
of September, 2005.


Carol M. Stanley
Notary Public of New Jersey
My Commission Expires November 18, 2005

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Colanhan

ASSIGNMENT

WHEREAS, we, Thomas J. Boyd, Guofeng Xu, Abdul Gaffar, David B. Vissio (below referred to as ASSIGNORS, residing, respectively, as set forth hereinafter, have made an invention for which application for Letters Patent of the United States was filed in the United States Patent and Trademark Office as Application Serial No. 10/601,474 filed June 23, 2003 naming the ASSIGNORS as an inventor, and entitled Oral Care Compositions Exhibiting Antiplaque and Breath Freshening Properties; and

WHEREAS, Colgate-Palmolive Company, a corporation duly organized and existing under the laws of the State of Delaware, United States of America and having its principal office and place of business at 300 Park Avenue, New York, New York 10022, and offices and place of business at 909 River Road, Piscataway, New Jersey 08855 (below referred to as "ASSIGNEE"), is desirous of obtaining the entire right, title and interest in and to the aforesaid invention and patent application and corresponding patent rights worldwide;

NOW, THEREFORE, in consideration of good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, ASSIGNORS, by these presents do sell, assign and transfer to ASSIGNEE, the full and exclusive right, title and interest in and to the aforesaid invention, the aforesaid U.S. and all corresponding foreign patent applications, all divisional, continuation, continuation-in-part, reissue and reexamination applications of the aforesaid U.S. application, and all Letters Patent or comparable rights issuing thereon in the United States and in all foreign countries, together with the right of priority under the International Convention for the Protection of Industrial Property, Inter-American Convention Relating to Patents, Designs and Industrial Models, and any other international agreements to which the United States of America adheres, and the ASSIGNORS hereby authorize and request the U.S. Commissioner of Patents and Trademarks and all foreign Patent Offices to issue all Letters Patent or comparable rights issuing on any application as aforesaid to ASSIGNEE, or to its successors, assigns or legal representatives;

ASSIGNORS hereby covenant that ASSIGNORS have full right to convey the entire interest herein assigned, and that ASSIGNORS have not executed, and will not execute, any agreement in conflict herewith;

ASSIGNORS agree to communicate to ASSIGNEE or to its successors, assigns or legal representatives any and all facts known to them or any of them respecting said invention, and without further remuneration to testify in any legal proceeding, sign all lawful papers, execute all divisional, continuation, continuation-in-part, reissue and reexamination applications, make all rightful oaths and generally do all lawful acts to aid ASSIGNEE or its successors, assigns or legal representatives to obtain and enforce proper patent protection for said invention in all countries and to enhance or perfect ASSIGNEE's title in and to the invention and patent rights therein.

ASSIGNORS hereby authorize attorneys for ASSIGNEE to enter on this document any applicable serial numbers and filing dates after ASSIGNORS' execution of this document.

This Assignment is effective as of June 23, 2003.

IN TESTIMONY WHEREOF, I hereunto set my hand and seal this 9 day of
September 2003.

Address:

Thomas J. Boyd
Thomas J. Boyd
17 Mustang Trail
Somerset, New Jersey 08873, USA

08873
9/8/03 TJB

State of New Jersey
County of Middlesex

On this 9 day of September 2003, before me, a Notary Public in and
for the State and County aforesaid, personally appeared the above signatory, known to me to be the
person of that name, who executed the foregoing instrument in my presence.

MARIA V. LOGATTO
Notary Public of New Jersey
My Commission Expires 8/8/2005

Maria V. Logatto
NOTARY PUBLIC

IN TESTIMONY WHEREOF, I hereunto set my hand and seal this 8 day of
September 2003.

Address:

Guofeng Xu
Guofeng Xu
35 Bank Street
Princeton, New Jersey 08542, USA

State of New Jersey
County of Middlesex

On this 8 day of September 2003, before me, a Notary Public in and
for the State and County aforesaid, personally appeared the above signatory, known to me to be the
person of that name, who executed the foregoing instrument in my presence.

MARIA V. LOGATTO
Notary Public of New Jersey
My Commission Expires 8/8/2005

Maria V. Logatto
NOTARY PUBLIC

IN TESTIMONY WHEREOF, I hereunto set my hand and seal this 8 day of
Sept 2003.

Address:

Abdul Gaffar
Abdul Gaffar
89 Carter Road
Princeton, New Jersey 08540, USA

State of New Jersey
County of Middlesex

On this 8 day of September 2003, before me, a Notary Public in and
for the State and County aforesaid, personally appeared the above signatory, known to me to be the
person of that name, who executed the foregoing instrument in my presence.

MARIA V. LOGATTO
Notary Public of New Jersey
My Commission Expires 8/8/2005

Maria V. Logatto
NOTARY PUBLIC

IN TESTIMONY WHEREOF, I hereunto set my hand and seal this 8 day of September 2003.

David B. Viscio
David B. Viscio
37 Norton Road
Monmouth Jct., New Jersey 08852, USA

Address:

State of New Jersey
County of Middlesex

On this 8 day of September 2003, before me, a Notary Public in and for the State and County aforesaid, personally appeared the above signatory, known to me to be the person of that name, who executed the foregoing instrument in my presence.

MARIA V. LOGATTO
Notary Public of New Jersey
My Commission Expires 8/8/2005

Maria V. Logatto
NOTARY PUBLIC

ASSIGNMENT

WHEREAS, we, Michael Prencipe, Thomas J. Boyd, M. Teresa R. Carale (below referred to as ASSIGNOR(S)), residing, respectively, as set forth hereinafter, have made an invention for which application for Letters Patent of the United States was filed in the United States Patent and Trademark Office as Application Serial No. 10/875,063 filed 6/23/2004 naming the ASSIGNOR(S) as an inventor, and entitled Stable Dentifrice Compositions and

WHEREAS, Colgate-Palmolive Company, a corporation duly organized and existing under the laws of the State of Delaware, United States of America and having its principal office and place of business at 300 Park Avenue, New York, New York 10022, and offices and place of business at 909 River Road, Piscataway, New Jersey 08855 (below referred to as "ASSIGNEE"), is desirous of obtaining the entire right, title and interest in and to the aforesaid invention and patent application and corresponding patent rights worldwide;

NOW, THEREFORE, in consideration of good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, ASSIGNORS, by these presents do sell, assign and transfer to ASSIGNEE, the full and exclusive right, title and interest in and to the aforesaid invention, the aforesaid U.S. and all corresponding foreign patent applications, all divisional, continuation, continuation-in-part, reissue and reexamination applications of the aforesaid U.S. application, and all Letters Patent or comparable rights issuing thereon in the United States and in all foreign countries, together with the right of priority under the International Convention for the Protection of Industrial Property, Inter-American Convention Relating to Patents, Designs and Industrial Models, and any other international agreements to which the United States of America adheres, and the ASSIGNORS hereby authorize and request the U.S. Commissioner of Patents and Trademarks and all foreign Patent Offices to issue all Letters Patent or comparable rights issuing on any application as aforesaid to ASSIGNEE, or to its successors, assigns or legal representatives;

ASSIGNORS hereby covenant that ASSIGNORS have full right to convey the entire interest herein assigned, and that ASSIGNORS have not executed, and will not execute, any agreement in conflict herewith;

ASSIGNORS agree to communicate to ASSIGNEE or to its successors, assigns or legal representatives any and all facts known to them or any of them respecting said invention, and without further remuneration to testify in any legal proceeding, sign all lawful papers, execute all divisional, continuation, continuation-in-part, reissue and reexamination applications, make all rightful oaths and generally do all lawful acts to aid ASSIGNEE or its successors, assigns or legal representatives to obtain and enforce proper patent protection for said invention in all countries and to enhance or perfect ASSIGNEE's title in and to the invention and patent rights therein.

ASSIGNORS hereby authorize attorneys for ASSIGNEE to enter on this document any applicable serial numbers and filing dates after ASSIGNORS' execution of this document.

This Assignment is effective as of June 23, 2004
(Date of Filing)

(Assignment con't)

IN TESTIMONY WHEREOF, I hereunto set my hand and seal this 12 day of October 2004.

Address:

Michael Pencipe
Michael Pencipe
39 Spruce Street
West Windsor, New Jersey 08550

State of New Jersey
County of Middlesex

On this 12 day of October 2004, before me, a Notary Public in and for the State and County aforesaid, personally appeared the above signatory, known to me to be the person of that name, who executed the foregoing instrument in my presence.

MARIA V. LOGATTO
Notary Public of New Jersey
My Commission Expires 8/8/2005

Maria V. Logatto
NOTARY PUBLIC

IN TESTIMONY WHEREOF, I hereunto set my hand and seal this 11 day of October 2004.

Address:

Thomas J. Boyd
Thomas J. Boyd
226 High Street
Metuchen, New Jersey 08840

State of New Jersey
County of Middlesex

On this 11 day of October 2004, before me, a Notary Public in and for the State and County aforesaid, personally appeared the above signatory, known to me to be the person of that name, who executed the foregoing instrument in my presence.

MARIA V. LOGATTO
Notary Public of New Jersey
My Commission Expires 8/8/2005

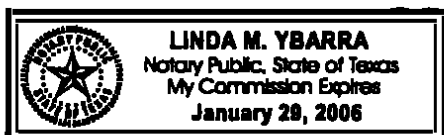
Maria V. Logatto
NOTARY PUBLIC

IN TESTIMONY WHEREOF, I hereunto set my hand and seal this 7 day of October 2004.

M. Teresa R. Carale
M. Teresa R. Carale
Address: 1959 University Boulevard
Houston, Texas 77030

State of ~~New Jersey~~ Texas
County of ~~Middlesex~~ Harris

On this 7th day of October 2004, before me, a Notary Public in and for the State and County aforesaid, personally appeared the above signatory, known to me to be the person of that name, who executed the foregoing instrument in my presence.



Linda M. Ybarra
NOTARY PUBLIC

Colgate-Palmolive Company accepts this Assignment.

COLGATE-PALMOLIVE COMPANY

By Ellen K. Park
Ellen K. Park
Associate General Counsel &
Chief Patent Counsel

TRADUCCIÓN AL ESPAÑOL del documento de cesión de solicitud de patente a
Colgate-Palmolive Company, firmado por los cedentes y el cesionario.

APOSTILLA

(Convención de La Haya del 5 de Octubre de 1961)

1. PAÍS: ESTADOS UNIDOS DE AMERICA
2. ESTE DOCUMENTO PÚBLICO HA SIDO FIRMADO POR:
ELAINE M. FLYNN
3. ACTUANDO EN CAPACIDAD DE:
FUNCIONARIO DEL CONDADO
4. LLEVA EL SELLO/TIMBRE DE:
CONDADO DE MIDDLESEX

CERTIFICADO

5. EN TRENTON, NEW JERSEY
6. EL 9 DE NOVIEMBRE DE 2005
7. POR John E. McCormac, CPA, TESORERO DE NEW JERSEY
8. NO. A243562
9. SELLO/TIMBRE
10. FIRMA

John E. McCormac (Firma)

CONDADO DE MIDDLESEX

ESTADO DE NEW JERSEY

ESTADOS UNIDOS DE AMERICA

Yo Kristyne A. Bullock, de COLGATE-PALMOLIVE COMPANY, declaro que la copia anexa al presente es una fotocopia verdadera de las cesiones como base de U.S. número de serie 10/601,474 presentada el 23 de junio de 2003 y U.S. número de serie 10/875,063 presentada el 23 de junio de 2004.

(Firma)

Kristyne A. Bullock
Abogado de Patentes

Suscrito y jurado
Ante mi este 30
de septiembre de 2005.

Carol M. Stanley (Firma)
Carol M. Stanley
Notario Público de New Jersey
Mi comisión expira el 18 de Noviembre de 2005.

ESTADO DE NEW JERSEY
Condado de Middlesex

Yo, Elaine M. Flinn, Funcionario del Condado de Middlesex, certifico que

CAROL M. STANLEY

Cuyo nombre aparece suscrito al certificado de prueba de reconocimiento del instrumento adjunto era al momento de tomar el mismo un

NOTARIO PUBLICO DE NEW JERSEY

Actuando en y para dicho condado, debidamente comisionada y juramentada, y calificada para actuar como tal; que como tal

NOTARIO PUBLICO DE NEW JERSEY

Estaba debidamente autorizada por las leyes del Estado de New Jersey para tomar y certificar declaraciones; para administrar juramentos y promesa solemnes; para tomar declaraciones juradas por escrito y certificar el reconocimiento y la prueba de instrumentos jurídicos y otros instrumentos escritos para tierras, arrendamientos y herencias ser leídos como evidencia o registrados en este estado; y además, que estoy familiarizada con la firma de tal

NOTARIO PUBLICO DE NEW JERSEY

Y verifico que la firma de tal prueba o reconocimiento es genuina.

EN TESTIMONIO DE LO CUAL, e firmado el presente y fijado el sello del Condado de Middlesex este 4 de noviembre de 2005.

Elaine M. Flinn (Firma)

CESIÓN

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CONSIDERANDO QUE, nosotros, Thomas J. Boyd, Goufeng Xu, Abdul Gaffar, David B. Viscio (referidos debajo como CEDENTES), residiendo, respectivamente, como se establece adelante, hemos hecho una invención para la cual se presentó solicitud de patente de Estados Unidos en la oficina de Marcas y Patentes de Estados Unidos como solicitud con número de serie 10/601,474 presentada el 23 de junio de 2003, nombrando a los CEDENTES como inventores y titulada Composiciones para el cuidado oral que exhiben propiedades antiplaca y de refrescar el aliento; y

CONSIDERANDO QUE, Colgate-Palmolive Company, una corporación debidamente organizada y existente bajo las leyes del Estado de Delaware, Estados Unidos de América y que tiene sus oficinas principales y lugar de operación en 300 Park Avenue, New York, New York 10022, y oficinas y lugar de operación en 909 River Road, Piscataway, New Jersey 08855 (referido debajo como CESIONARIO), tiene deseos de obtener la totalidad del derecho, título e intereses en y para la invención y solicitud de patente mencionadas arriba y los correspondientes derechos de patente alrededor del mundo.

AHORA, POR LO TANTO, en consideración de la consideración buena y valiosa, el recibo y la suficiencia de la cual se reconocen, los CEDENTES, por la presente venden, ceden y transfieren al CESIONARIO el derecho, título e interés completo y exclusivo en y para la invención arriba mencionada, la solicitud de patente de los Estados Unidos arriba mencionada y todas las solicitudes de patente extranjeras correspondientes, todas las solicitudes de división, continuación, continuación parcial, reemisión y reexaminación de la solicitud de patente de los Estados Unidos arriba mencionada, y todas las Patentes o derechos comparables emitidos sobre la misma en los Estados Unidos y en todos los países extranjeros, junto con el derecho de prioridad bajo la Convención Internacional para la Protección de la Propiedad Industrial, la Convención Interamericana Relacionada con Patentes, Diseños y Modelos Industriales, u cualquier otro acuerdo internacional al cual se adhieran los Estados Unidos, y los CEDENTES por la presente autorizan y solicitan al Comisionado de Marcas y Patentes de los Estados Unidos y a todas las Oficinas de Patentes extranjeras a emitir todas las patentes o derechos comparables que puedan surgir de cualquier solicitud al CESIONARIO, o sus sucesores, cesionarios o representantes legales;

Los CEDENTES garantizan que los CEDENTES tienen pleno derecho para comunicar la totalidad del interés aquí cedido, y que los CEDENTES no han ejecutado, y no ejecutarán, ningún acuerdo en conflicto con el presente;

Los CEDENTES acuerdan comunicar al CESIONARIO o a sus sucesores, cesionarios o representantes legales cualquiera y todos los hechos conocidos por ellos o por cualquiera de ellos respecto a dicha invención, y sin remuneración adicional testificar en cualquier proceso legal, firmar todos los papeles legales, ejecutar todas las solicitudes de división, continuación, continuación parcial, reemisión y reexaminación, hacer todos los juramentos correctos y en general hacer todos los actos legales para ayudar al CESIONARIO o sus sucesores, cesionarios o representantes legales a obtener y hacer valer la protección de patente para dicha invención en todos los países y a mejorar o perfeccionar el derecho del CESIONARIO en y para la invención y los derechos de patente de la misma.

Los CEDENTES por la presente autorizan a los abogados del CESIONARIO a ingresar en este documento cualquier número de serie y fecha de presentación aplicable después que el CEDENTE ha ejecutado este documento.

Esta cesión es efectiva desde: Junio 23 de 2003

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EN TESTIMONIO DE LO CUAL he puesto mi firma y fijado mi sello este 9 de septiembre de 2003

(Firma)
Thomas J. Boyd
Dirección: 17 Mustang Trail
Somerset, New Jersey 08873, EE.UU.

Estado de New Jersey
Condado de Middlesex

Este 9 de septiembre de 2003, ante mi, un notario público en y para el Estado y Condado arriba mencionados, apareció personalmente el arriba firmante, a quien conozco como la persona de ese nombre quien ejecutó el instrumento anterior en mi presencia.

MARIA V. LOGATTO
Notario Público de New Jersey
Mi comisión expira 8/8/2005

(Firma)
NOTARIO PUBLICO

EN TESTIMONIO DE LO CUAL he puesto mi firma y fijado mi sello este 8 de septiembre de 2003:

(Firma)
Guofeng Xu
Dirección: 35 Bank Street
Princeton, New Jersey 08542, EE.UU.

Estado de New Jersey
Condado de Middlesex

Este 8 de septiembre de 2003, ante mi, un notario público en y para el Estado y Condado arriba mencionados, apareció personalmente el arriba firmante, a quien conozco como la persona de ese nombre quien ejecutó el instrumento anterior en mi presencia.

MARIA V. LOGATTO
Notario Público de New Jersey
Mi comisión expira 8/8/2005

(Firma)
NOTARIO PUBLICO

EN TESTIMONIO DE LO CUAL he puesto mi firma y fijado mi sello este 8 de septiembre de 2003:

(Firma)
Abdul Gaffar
Dirección: 89 Carter Road
Princeton, New Jersey 08540, EE.UU.

Estado de New Jersey
Condado de Middlesex

Este 8 de septiembre de 2003, ante mi, un notario público en y para el Estado y Condado arriba mencionados, apareció personalmente el arriba firmante, a quien conozco como la persona de ese nombre quien ejecutó el instrumento anterior en mi presencia.

MARIA V. LOGATTO
Notario Público de New Jersey
Mi comisión expira 8/8/2005

(Firma)
NOTARIO PUBLICO

121

121

EN TESTIMONIO DE LO CUAL he puesto mi firma y fijado mi sello este 8 de septiembre de 2003

Dirección: (Firma)
David B. Viscio
37 Norton Road
Monmouth Jct., New Jersey 08852, EE.UU.

Estado de New Jersey
Condado de Middlesex

Este 8 de septiembre de 2003, ante mi, un notario público en y para el Estado y Condado arriba mencionados, apareció personalmente el arriba firmante, a quien conozco como la persona de ese nombre quien ejecutó el instrumento anterior en mi presencia.

MARIA V. LOGATTO
Notario Público de New Jersey
Mi comisión expira 8/8/2005

(Firma)
NOTARIO PUBLICO

CESIÓN

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CONSIDERANDO QUE, nosotros, Michael Principe, Thomas J. Boyd, M. Teresa R. Carale (referidos debajo como CEDENTES), residiendo, respectivamente, como se establece adelante, hemos hecho una invención para la cual se presentó solicitud de patente de Estados Unidos en la oficina de Marcas y Patentes de Estados Unidos como solicitud con número de serie 10/875,063 presentada el 6/23/2004, nombrando a los CEDENTES como inventores y titulada Composiciones dentífricas estables; y

CONSIDERANDO QUE, Colgate-Palmolive Company, una corporación debidamente organizada y existente bajo las leyes del Estado de Delaware, Estados Unidos de América y que tiene sus oficinas principales y lugar de operación en 300 Park Avenue, New York, New York 10022, y oficinas y lugar de operación en 909 River Road, Piscataway, New Jersey 08855 (referido debajo como CESIONARIO), tiene deseos de obtener la totalidad del derecho, título e intereses en y para la invención y solicitud de patente mencionadas arriba y los correspondientes derechos de patente alrededor del mundo.

AHORA, POR LO TANTO, en consideración de la consideración buena y valiosa, el recibo y la suficiencia de la cual se reconocen, los CEDENTES, por la presente venden, ceden y transfieren al CESIONARIO el derecho, título e interés completo y exclusivo en y para la invención arriba mencionada, la solicitud de patente de los Estados Unidos arriba mencionada y todas las solicitudes de patente extranjeras correspondientes, todas las solicitudes de división, continuación, continuación parcial, reemisión y reexaminación de la solicitud de patente de los Estados Unidos arriba mencionada, y todas las Patentes o derechos comparables emitidos sobre la misma en los Estados Unidos y en todos los países extranjeros, junto con el derecho de prioridad bajo la Convención Internacional para la Protección de la Propiedad Industrial, la Convención Interamericana Relacionada con Patentes, Diseños y Modelos Industriales, u cualquier otro acuerdo internacional al cual se adhieran los Estados Unidos, y los CEDENTES por la presente autorizan y solicitan al Comisionado de Marcas y Patentes de los Estados Unidos y a todas las Oficinas de Patentes extranjeras a emitir todas las patentes o derechos comparables que puedan surgir de cualquier solicitud al CESIONARIO, o sus sucesores, cesionarios o representantes legales;

Los CEDENTES garantizan que los CEDENTES tienen pleno derecho para comunicar la totalidad del interés aquí cedido, y que los CEDENTES no han ejecutado, y no ejecutarán, ningún acuerdo en conflicto con el presente;

Los CEDENTES acuerdan comunicar al CESIONARIO o a sus sucesores, cesionarios o representantes legales cualquiera y todos los hechos conocidos por ellos o por cualquiera de ellos respecto a dicha invención, y sin remuneración adicional testificar en cualquier proceso legal, firmar todos los papeles legales, ejecutar todas las solicitudes de división, continuación, continuación parcial, reemisión y reexaminación, hacer todos los juramentos correctos y en general hacer todos los actos legales para ayudar al CESIONARIO o sus sucesores, cesionarios o representantes legales a obtener y hacer valer la protección de patente para dicha invención en todos los países y a mejorar o perfeccionar el derecho del CESIONARIO en y para la invención y los derechos de patente de la misma.

Los CEDENTES por la presente autorizan a los abogados del CESIONARIO a ingresar en este documento cualquier número de serie y fecha de presentación aplicable después que el CEDENTE ha ejecutado este documento.

Esta cesión es efectiva desde: Junio 23 de 2004

(Fecha de presentación)

123

123

EN TESTIMONIO DE LO CUAL he puesto mi firma y fijado mi sello este 12 de octubre de 2004.

(Firma)
Michael Prencipe
Dirección: 39 Spruce Street
West Windsor, New Jersey 08550

Estado de New Jersey
Condado de Middlesex

Este 12 de octubre de 2004, ante mi, un notario público en y para el Estado y Condado arriba mencionados, apareció personalmente el arriba firmante, a quien conozco como la persona de ese nombre quien ejecutó el instrumento anterior en mi presencia.

MARIA V. LOGATTO
Notario Público de New Jersey
Mi comisión expira 8/8/2005
(Firma)
NOTARIO PUBLICO

EN TESTIMONIO DE LO CUAL he puesto mi firma y fijado mi sello este 11 de octubre de 2004.

(Firma)
Thomas J. Boyd
Dirección: 226 High Street
Metuchen, new jersey, 08840

Estado de New Jersey
Condado de Middlesex

Este 11 de octubre de 2004, ante mi, un notario público en y para el Estado y Condado arriba mencionados, apareció personalmente el arriba firmante, a quien conozco como la persona de ese nombre quien ejecutó el instrumento anterior en mi presencia.

MARIA V. LOGATTO
Notario Público de New Jersey
Mi comisión expira 8/8/2005
(Firma)
NOTARIO PUBLICO

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EN TESTIMONIO DE LO CUAL he puesto mi firma y fijado mi sello este 7 de octubre de 2004.

Dirección: (Firma)
M. Teresa R. Carale
1959 University Boulevard
Houston, texas 77030

Estado de Texas
Condado de Harris

Este 7 de octubre de 2004, ante mi, un notario público en y para el Estado y Condado arriba mencionados, apareció personalmente el arriba firmante, a quien conozco como la persona de ese nombre quien ejecutó el instrumento anterior en mi presencia.

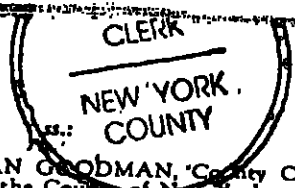
LINDA M. YBARRA (Firma)
Notario Público, Estado de Texas NOTARIO PUBLICO
Mi comisión expira Enero 28 de 2006

Colgate-Palmolive acepta esta cesión.

COLGATE-PALMOLIVE COMPANY

Por: (Firma)
Ellen K. Park
Abogado general asociado
Abogado en jefe de patentes

128 125



252373 Form 1

I, NORMAN GOODMAN, County Clerk and Clerk of the Supreme Court of the State of New York, in and for the County of New York, a Court of Record, having by law a seal, DO HEREBY CERTIFY pursuant to the Executive Law of the State of New York, that

Rosie S. Dizon

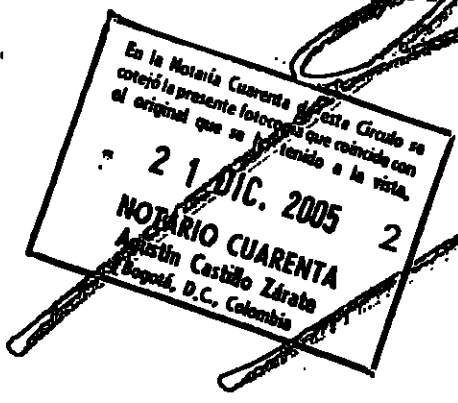
whose name is subscribed to the annexed affidavit, deposition, certificate of acknowledgment or proof, was at the time of taking the same a NOTARY PUBLIC in and for the State of New York duly commissioned, sworn and qualified to act as such; that pursuant to law, a commission or a certificate of his official character, with his autograph signature has been filed in my office; that at the time of taking such proof, acknowledgment or oath, he was duly authorized to take the same; that I am well acquainted with the handwriting of such NOTARY PUBLIC or have compared the signature on the annexed instrument with his autograph signature deposited in my office, and I believe that such signature is genuine.

IN WITNESS WHEREOF, I have hereunto set my hand affixed my official seal this

OCT 30 2001

FEE PAID \$3.00

Norman Goodman
County Clerk and Clerk of the Supreme Court, New York County



Apostille

(Convention de La Haye du 5 Octobre 1961)

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1. Country: **United States of America**
This public document
2. has been signed by **Norman Goodman**
3. acting in the capacity of **County Clerk**
4. bears the seal/stamp of the county of **New York**

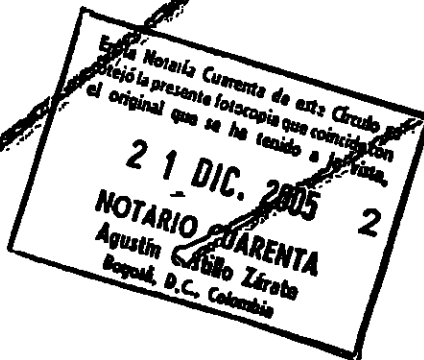
Certified

5. At New York, New York
6. the 30th day of October 2001
7. by Special Deputy Secretary of State, State of New York
8. No. NYC-9786540B
9. Seal/Stamp
10. Signature

Aqil M. Qureshi

Aqil M. Qureshi
Special Deputy Secretary of State

04135585.RSL (REV: 2/8/98)



Brigard & Castro

SANTA FE DE BOGOTA - COLOMBIA

PODER

POWER OF ATTORNEY

127

Yo (nosotros)

domiciliado(s) en

Nombro(amos) a: RAMIRO CASTRO DUQUE y/o JUAN PABLO CADENA SARMIENTO y/o BEATRIZ JARAMILLO S.

de Santafé de Bogotá, Colombia, apoderados verdaderos y legales con poder especial, amplio y suficiente, para recabar de las oficinas y autoridades colombianas administrativas, judiciales y de policía, en cualquier instancia o recurso, la obtención de patentes de invención, registros de marcas, diseños industriales, modelos de utilidad, depósitos de nombres comerciales y enseñanzas, registros de derechos de autor y contratos sobre los mismos, obtención de certificados de obtentor de variedades vegetales, así como sus prórrogas, renovaciones, anotaciones de traspaso, cambios de nombre y/o domicilio; elaborar, tramitar y registrar contratos de licencia y licencias de cualesquiera clases; intervenir como demandante o como demandado en cualquier instancia y recurso ante cualquier juez, corporación, funcionario público o autoridad en acciones judiciales, administrativas y de policía tales como: oposiciones al registro de marcas; acciones de caducidad, cancelación y nulidad; acciones reivindicatorias, acciones derivadas de la obtención o explotación de licencias; acciones de competencia desleal; demandas penales; acciones de indemnización de perjuicios, reclamos y observaciones a solicitudes de patentes, diseños industriales, modelos de utilidad, en el ejercicio de medidas cautelares y en otras acciones o medidas similares.

A este efecto, lo(s) faculto(amos) para elevar solicitudes, formular descripciones, enmiendas, protestas, declaraciones, oposiciones, cancelaciones, nulidades, apelaciones y reclamos; pagar impuestos, cuotas y gravámenes prescritos por la ley; renunciar o desistir a derechos concedidos o en curso de concesión; recibir toda clase de documentos y valores, dando el descargo respectivo, y, en general, para dar ante dichas autoridades todos los pasos necesarios al efecto indicado y tomar todas las medidas que creyeren conducentes al resguardo de mis (nuestros intereses), con todas las demás facultades legales necesarias.

Este poder comprende la facultad de ratificar o confirmar en mi (nuestro) nombre lo actuado así como la facultad de desistir, transigir, comprometer, y la de sustituirlo en todo o en parte y revocar sustituciones. Asimismo nombro(amos) a: RAMIRO CASTRO DUQUE y/o JUAN PABLO CADENA SARMIENTO y/o BEATRIZ JARAMILLO S. domiciliado(s) en la Carrera 7 No. 16-56 Piso 9, mis (nuestros) apoderados en Colombia, con facultades para recibir notificaciones y designar apoderados judiciales o extrajudiciales.

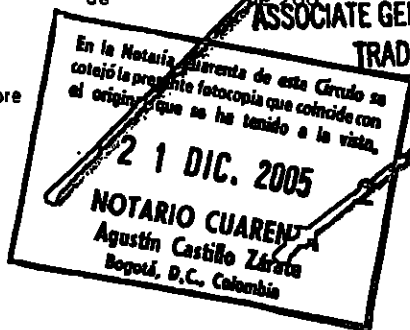
Otorgado y firmado en

hoy

de

Firma

Nombre



VICE PRESIDENT &
ASSOCIATE GENERAL COUNSEL
TRADEMARK

I (We)

COLGATE-PALMOLIVE COMPANY, a Delaware corporation, of 300 Park Avenue, New York, New York 10022, U. S. A.

Hereby appoint RAMIRO CASTRO DUQUE and/or JUAN PABLO CADENA SARMIENTO and/or BEATRIZ JARAMILLO S.

of Santafé de Bogotá, Colombia, my (our) true and lawful attorneys with special, ample and sufficient power to obtain from the Colombian administrative, judicial and police offices and authorities, in any instance, privileges of patents of invention, registration of trademarks, industrial designs and utility models; registration of commercial names and emblems, registration of copyright and contracts related thereto, certificates of obtainers of vegetable varieties, as well as extensions, renewals and recordal of assignments and changes of name and domicile related to the above; to prepare, prosecute and register licenses of any kind; to act as plaintiff or defendant in any instance or recourse, and before any judge, corporation, public official or authority in judicial, administrative and police actions, such as: oppositions to the registration of trademarks; caducity, cancellation and nullity actions; claim actions derived from the obtaining or exploitation of licenses, action of unfair competition; penal demands, actions of indemnities for damages; claims or observations on patent applications, models, industrial designs and utility models; in the exercise of preventive measures; and in other actions or similar proceedings.

To that effect they are hereby empowered to file applications, formulate descriptions, amendments, protests, declarations, oppositions, cancellations, nullities, appeals and claims; to pay taxes, quotas and assessments prescribed by law, renounce or waive the rights granted or in the process of granting; to receive all kind of documents and valuables, giving the respective release of receipt, and, in general, to take before said authorities the necessary steps to such effect, and any measures that they may deem pertinent to the safeguard of my (our) interest(s) with all the other necessary legal powers.

This power includes the faculty to ratify or confirm desist, settle and compromise on my (our) behalf, and to substitute this power in whole or in part and to revoke substitutions. At the same time I (We) hereby appoint RAMIRO CASTRO DUQUE and/or JUAN PABLO CADENA SARMIENTO and/or BEATRIZ JARAMILLO S.

domiciled in Carrera 7 No. 16-56, Piso 9, my (our) attorney(s) in fact, with powers to receive notifications and to designate judicial and extrajudicial attorneys.

Granted and signed in New York, N.Y.

this 29 day of 2001

Signature

Name

SCOTT E THOMPSON

CERTIFICADO NOTARIAL (SOCIEDAD)

NOTARIAL CERTIFICATE (CORPORATION)

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Hoy de de
personalmente compareció ante mí

a quien conozco, y de quien me consta que firmó el anterior documento, debidamente juramentado declaró y dijo que él es

de

Sociedad legalmente constituida para un periodo de duración que aún no ha terminado; que el declarante está autorizado por dicha compañía para conferir este poder; que el sello estampado por él al pie de tal poder, en nombre y representación de la expresada compañía, es el sello oficial de ella; y que el objeto para el cual se confiere este instrumento está comprendido dentro del de la sociedad.

El suscrito Notario hace constar que tuvo a la vista las pruebas de la existencia de la sociedad.

Estado de
con fecha

y que quien confiere el presente poder es su representante.

On this OCT 29 2001 day of
personally appeared before me

SCOTT E THOMPSON

to me known, and known to me to be the person who signed the foregoing instrument who being by me duly sworn did depose and say that he (she) is the

**VICE PRESIDENT &
ASSOCIATE GENERAL COUNSEL
TRADEMARK**

COLGATE-PALMOLIVE COMPANY

Which is legally constituted for a term not yet expired, that deponent is authorized by said Company to confer this Power of Attorney: that the seal affixed hereunto by the deponent in the name and on behalf of said Corporation is the corporate seal thereof; and that the purpose for which this instrument is granted is included within the corporate purpose of company.

The undersigned Notary Public attests that he has seen the documents that prove the existence of the company.

State of Delaware
under date of May 13, 1997

and that he (she) who grants the present power of attorney is its Representative.

Notario Público (sello)

Rosie S. Dizon
Notary Public (Seal)

**CERTIFICADO NOTARIAL
PERSONA NATURAL**

ROSIE S. DIZON
Notary Public, State of New York
No. 31-4941117
Qualified in New York County
Commission Expires Aug. 15, 2002

COUNTY

Hoy de de , compareció(eron)
ante mí

On this OCT 29 2001 day of
personally appeared before me

SCOTT E THOMPSON

a quien (es) conozco y me consta que es(son) la(s) persona(s) firmante(s) del documento que precade y quien(es) declara(n) que otorgan el mismo para los fines y propósitos que en él se expresan.

who is(are) known to me and who I attest executed the foregoing document and he (they) declared he (they) grant(s) the document for the uses and purposes therein expressed.

Notario Público (sello)

Rosie S. Dizon
Notary Public (Seal)

LEGALIZACION POR APOSTILLA ES REQUERIDA

En la Notaría Pública de este Estado se
cotejó la presente fotocopia que coincide con
el original que se ha tenido a la vista.
21 DIC. 2005
NOTARIO CUARENTA
Agustín Castillo Zúñiga
Bogotá, D.C.

ROSIE S. DIZON
Notary Public, State of New York
No. 31-4941117
Qualified in New York County
Commission Expires Aug. 15, 2002

122

129

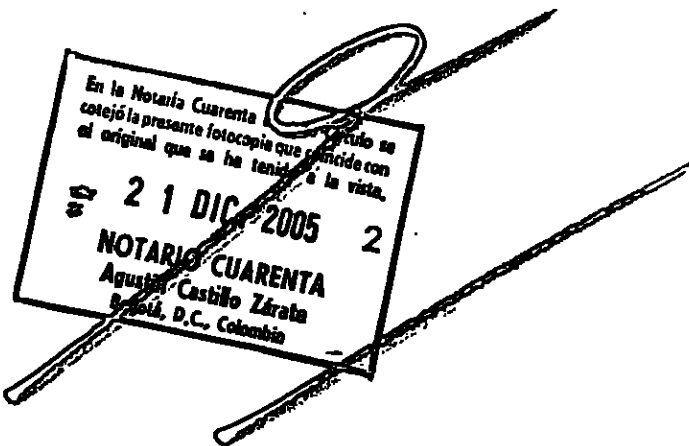
APOSTILLE

(Convención de La Haya del 5 de Octubre de 1961)

1. País: ESTADOS UNIDOS DE AMERICA
Este documento público
2. ha sido firmado por **Norman Goodman**
3. actuando en capacidad de **Oficial del Condado**
4. lleva el sello/timbre del condado de New York

CERTIFICADO

5. en New York, New York
6. el 30 de Octubre de 2001
7. por Secretario de Estado Encargado Especial, Estado de New York
8. No. NYC-9786540B
9. Sello/Timbre
10. Firma
(Firma)
Aquil M. Qureshi
Secretario de Estado Encargado Especial



✓ 130

Estado de New York)
) ss.
Condado de New York)

252373

Rosie S. Dizon

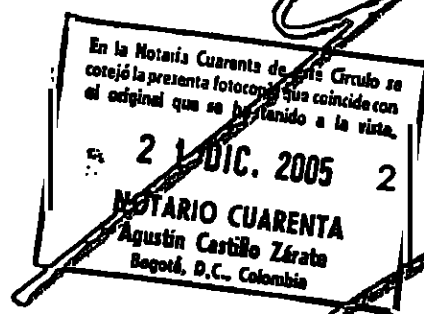
COMO TESTIGO DE LO MISMO, he fijado al presente mi firma t mi sello
oficial este

30 de Octubre de 2001

TARIFA PAGADA \$3.00

(Firma)

Oficial del Condado, Oficial de la Corte Suprema, Condado de New York





GAVIRI

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ORGANIZACION ELECTORAL
REGISTRADURÍA NACIONAL DEL ESTADO CIVIL

REGISTRO CIVIL DE DEFUNCIÓN

Indicativo
Serial 5562241

Datos de la oficina de registro																									
Clase de oficina:		Registraduría		Notaría		X		Consulado		Corregimiento		Insp. de Policía		Código		999b									
País - Departamento - Municipio - Corregimiento o/o Inspección de Policía																									
COLOMBIA CUNDINAMARCA BOGOTA D..C NOTARIA 32.																									
Datos del inscrito																									
Apellidos y nombres completos																									
CASTRO DUQUE RAMIRO																									
Documento de identificación (Clase y número)										Sexo (en Letras)															
C.C.No. 170322 DE BOGOTA										MASCULINO															
Datos de la defunción																									
Lugar de la Defunción: País - Departamento - Municipio - Corregimiento o/o Inspección de Policía																									
COLOMBIA CUNDINAMARCA BOGOTA D.C.																									
Fecha de la defunción										Hora		Número de certificado de defunción													
Año		2		0		0		4		Mes		1		0		Día		3		0		04:10 PM		A- 2094375.	
Presunción de muerte																									
Lugado que profiere la sentencia										Fecha de la sentencia															
Año																									
Documento presentado										Nombre y cargo del funcionario															
Autorización Judicial												Certificado Médico		X		ANDRES DIAZ CAMPOS.-									
														R.M.No. 79982662											
Datos del denunciante																									
Apellidos y nombres completos																									
EDGAR DAVID REGINO II.																									
Documentos de identificación (Clase y número)										Firma															
C.C.No. 15.030.154 DE LORICA/ CORDOBA																									
Primer testigo																									
Apellidos y nombres completos																									
Documentos de identificación (Clase y número)																									
Firma																									
Segundo testigo																									
Apellidos y nombres completos																									
Documentos de identificación (Clase y número)																									
Firma																									
Fecha de inscripción										Nombre y firma del funcionario que autoriza															
Año		2		0		0		4		Mes		1		Día		0		2		BLANCA ROSA REPREPO					
PADRES: ALFON SO CASTRO																									
MERCEDES DUQUE.																									
ESPACIO PARA NOTAS																									

ORIGINAL PARA LA OFICINA DE REGISTRO

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NOTARIA 32

DEL CÍRCULO DE SANTA FE DE BOGOTÁ, D.C.

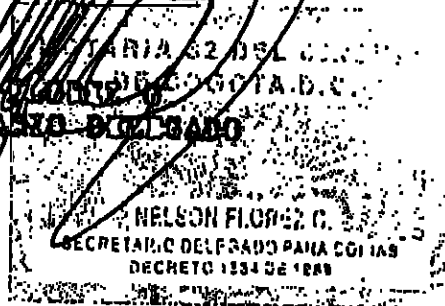
Germán Eleázar Moreno L.
Notario

**COMO SECRETARIO DELEGADO DE LA NOTARIA TREINTA Y DOS (32) DEL
CÍRCULO DE BOGOTÁ**

CERTIFICO, QUE:

La presente acta es fiel copia del original tomada del registro
civil de defunciones serial indicativo número: **562201**
que expido en la ciudad de Bogotá D.C., hoy: **05 NOV. 2004**

SECRETARIO DELEGADO



REQUISITOS NECESARIOS PARA PRESENTACION Y AGILIZACION DEL TRAMITE

	USUARIO	RADICADOR
PATENTE DE INVENCION ✓	()	()
MODELO DE UTILIDAD	()	()
- Indicación de que se solicita la concesión de una patente. ✓	()	()
- Datos de identificación del solicitante o de la persona que se 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 o 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 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:

[Firma]
Dic 22 de 2005