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(57) Abstract

This invention involves a composition for treating or preventing dental plaque, calculus and gingivitis, or malodor of the oral cavity, comprising: (a) (i) a source of a safe and effective amount of zinc ions; (ii) a source of citrate ions; and (iii) one or more anticalculus agents selected from the group consisting of pyrophosphate, phosphonate, diphosphonate and pharmaceutically-acceptable linear condensed polyphosphates of the general formula: $(P_nO_{(3n+1)}^{(n+2)-}$ wherein n is an integer from 2 to 21; wherein the molar ratio of zinc:citrate is at most about 1:1; the molar ratio of zinc:pyro is at most about 1:1; and (b) and a pharmaceutically-acceptable topical oral carrier. This invention also involves methods for treating or preventing dental plaque, calculus and gingivitis, or malador of the oral cavity, comprising administering to the oral cavity of a human or other animal such a composition.

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ORAL COMPOSITIONS CONTAINING ANTIPLAQUE, ANTICALCULUS AGENTS

The subject invention relates to oral compositions, such as dentifrices and oral solutions, for the treatment or prevention of dental plaque, calculus and gingivitis, and mouth malodor.

Background of the Invention

The mouth is a habitat for microbial growth and colonization. Within the mouth, the gums, lips, oral mucosa (cheek), palate, tongue and teeth provide surfaces for the colonization and accumulation of bacteria. Teeth are unique in the oral cavity because they have hard, non-shedding surfaces where bacteria and their products (dental plaque) can significantly accumulate, especially in approximal areas and along the gingival crevice.

Dental plaque is a rough sticky film on the teeth that is made up of saliva, bacteria and food particles which adheres tenaciously to teeth at points of irregularity or discontinuity. Within a few hours of teeth cleaning, a film of salivary mucins, consisting primarily of proteins, forms on the teeth. Various oral bacteria colonize the mucins and multiply, forming a layer of plaque. Carbohydrate food debris adheres to the mucins and is digested by some types of plaque-causing bacteria. The digestion both produces by-products which add to the plaque, and produces acid which erodes tooth enamel. The bacterial by-products produced in the oral cavity also include foul smelling gases which can result in malodor of the oral cavity.

The oral bacteria in dental plaque includes many gram positive and gram negative microorganisms embedded in an extracellular matrix of insoluble polysaccharides, firmly attached to teeth and other oral surfaces. The colonization of bacteria to form dental plaque follows an ecological pattern where a few pioneer aerobic species, mostly gram-positive streptococci, colonize enamel surfaces. The plaque then progresses through stages of increasing microbial complexity. Mature plaques, often found in protected regions of the

teeth, such as cracks, approximal regions and in the gingival crevice, typically contain anaerobes. Saliva and crevicular fluid are a source of nutrients for the dental plaque. Local conditions affect the metabolic activity and composition of dental plaque.

If not prevented or removed, plaque may become embedded with mineral salts, containing calcium and phosphate, to form a hard crusty deposit, calculus or tartar, on the teeth. Calculus may be white or yellowish in color or may be stained or discolored by extraneous agents. Calculus tends to be more unsightly than plaque and much more difficult to remove from the teeth. The toxins in plaque and calculus can irritate the gingival tissues surrounding the coated teeth, causing inflammation and destruction of the gums which can lead to other complications.

Zinc is an anticalculus agent; however, compositions containing zinc generally taste astringent and unpleasantly bitter. Like the chemical and biological activities, the negative aesthetics of the zinc cation are dose dependent: higher concentrations of zinc exhibit poorer aesthetics; therefore, increasing the concentration of free zinc tends to increase efficacy at the expense of aesthetics. This coupled behavior between efficacy and aesthetics has limited the utility of zinc in oral compositions. Pyrophosphate is also an anticalculus agent and, likewise, has an unpleasant taste which worsens with increased pyrophosphate concentration. By carefully formulating zinc and pyrophosphate-containing compositions, applicants have surprisingly found that the level of zinc in an oral composition can be increased, thus increasing the corresponding anticalculus effect, without greatly increasing the negative aesthetics of the composition.

It has been surprisingly found that it is possible to uncouple the efficacy and aesthetics of zinc containing compositions. When zinc is formulated with citrate and pyro at certain ratios of zinc:citrate and zinc:pyro, it is possible to avoid the aesthetic negatives typically associated with the zinc ion.

It is an object of the subject invention to provide compositions for impeding calculus formation in the oral cavity.

It is also an object of the subject invention to provide compositions for impeding dental plaque formation in the oral cavity.

It is a further object of the subject invention to provide methods for impeding calculus formation in the oral cavity.

It is also an object of the subject invention to provide methods for impeding dental plaque formation in the oral cavity.

Summary of the Invention

This invention involves a composition for treating or preventing dental plaque, calculus and gingivitis, or malodor of the oral cavity, comprising:

(a) (i) a source of a safe and effective amount of zinc ions; (ii) a source of citrate ions; and (iii) one or more anticalculus agents selected from the group consisting of pyrophosphate, phosphonate, diphosphonate and pharmaceutically-acceptable linear condensed poly-phosphates of the general formula: $(P_nO_{(3n+1)})^{(n+2)-}$ wherein n is an integer from 2 to 21;

wherein the molar ratio of zinc:citrate is at most about 1:1; the molar ratio of zinc:pyro is at most about 1:1; and

(b) and a pharmaceutically-acceptable topical oral carrier.

This invention also involves methods for treating or preventing dental plaque, calculus and gingivitis, or malodor of the oral cavity, comprising administering to the oral cavity of a human or other animal such a composition.

Detailed Disclosure of the Invention

The subject invention provides compositions effective against dental plaque formation, calculus formation, gingivitis, and mouth malodor.

"Pharmaceutically-acceptable topical oral carrier", as used herein, denotes a carrier for the active compounds of the subject invention (hereinafter "Actives") comprising solid or liquid filler diluents suitable for use in contact with the oral tissues of humans and lower animals without undue toxicity, incompatibility, instability, irritation, allergic response, and the like, commensurate with a reasonable benefit/risk ratio. Such topical oral carrier, when combined with Actives of the subject invention, results in a composition which is administered topically to the oral cavity. Preferably such compositions are held in the oral cavity for a period of time, and then largely

expectorated rather than being swallowed. Such compositions include mouthwashes, mouth rinses, mouth sprays, dental treatment solutions, toothpastes, dental gels, tooth powders, prophylaxis pastes, lozenges, chewing gums and the like and are more fully described hereinafter. Dentifrices and mouthwashes are the preferred compositions.

"Pyro", as used herein, refers to pyrophosphate; phosphonate; diphosphonate; and pharmaceutically-acceptable polyphosphates including, but not limited to, linear condensed polyphosphates of the general formula: $(P_nO_{(3n+1)})^{(n+2)-}$ wherein n is an integer from 2 to 21.

"Free pyro", as used herein, refers to pyro that is not bound or chelated to the transition metal, zinc.

"Free zinc", as used herein, refers to hydrated zinc cationic species, such as $Zn(H_2O)_6^{2+}$.

As used herein, percentages listed are weight percentage of composition unless otherwise specified.

The amounts of pyro and citrate are expressed in terms of a ratio to the amount of zinc in the oral composition. On a molar basis, the amount of citrate relative to zinc is at least one when the molar amount of zinc is one (*i.e.* the molar ratio of zinc:citrate is at most about 1:1); and the amount of pyro relative to zinc is at least one when the molar amount of zinc is one (*i.e.* the molar ratio of zinc:pyro is at most about 1:1). Preferably the zinc:citrate ratio is from about 1:1 to about 1:20; more preferably from about 1:1 to about 1:4, more still preferably from about 1:1 to about 1:3. Preferred is a zinc:pyro ratio from about 1:1 to about 1:20 more preferably from about 1:1 to about 1:8, more preferably still from about 1:1.5 to about 1:6. Also preferred is a zinc:citrate:pyro ratio wherein the sum of the molar ratio amounts of citrate ions and pyro ions is from about 2 to about 9, more preferably from about 3 to about 9, when the ratio amount of zinc is 1.

The amount of zinc suitable for the purposes of the subject invention is from about 0.005% to about 5% Zn; more preferably from about 0.03% to about 3% Zn; more preferably still from about 0.05% to about 2% Zn. In dentifrice compositions, the preferred amounts of zinc are from about 0.1% to about 2%, more preferably from about 0.25% to about 1%. In mouthwashes, mouth rinses, mouth sprays and

dental solutions, the preferred amount of zinc is from about 0.005% to about 1%, more preferably from about 0.05% to about 0.5%.

The amount of citrate anion suitable for the purposes of the subject invention is from about 0.015% to about 25% citrate. In dentifrice compositions, the preferred amounts of citrate anion are from about 0.2 % to about 17%, more preferably from about 0.7% to about 12%, more preferably still from about 1.5% to about 5%. In mouthwashes, mouth rinses, mouth sprays and dental solutions, the preferred amount of citrate anion is from about 0.01% to about 12%, more preferably from about 0.1% to about 6%, more preferably still from about 0.15% to about 1%.

The amount of pyro anion suitable for the purposes of the subject invention is from about 0.015% to about 25% pyro. In dentifrice compositions, the preferred amounts of pyro ion are from about 0.25% to about 16%, more preferably from about 0.6% to about 11%. In mouthwashes, mouth rinses, mouth sprays and dental solutions, the preferred amount of pyro anion is from about 0.01% to about 11%, more preferably from about 0.1% to about 5%.

Suitable sources of zinc ions include zinc oxides, zinc halides, zinc-strong acid complexes, $Zn(NO_3)_2$, $Zn(ClO_4)_2$, $ZnSO_4$, and zinc-organic acids sources such as zinc lactate, tartrate, citrate salts, zinc citrate trihydrate and sodium zinc citrate. Zinc sources that are unacceptable are zinc ethylenediaminetetraacetate (ZnEDTA) and zinc nitrilotriacetate (ZnNTA). Preferred sources of zinc ions include zinc oxide (ZnO) and zinc nitrate; more preferred is ZnO.

Suitable sources of citrate ions include zinc citrate; citric acid; alkali metal salts of citric acid, especially sodium citrate and potassium citrate; pharmaceutically acceptable hydrated and dehydrated salts of any of the above; and mixtures of any of the above.

Suitable sources of pyro ions are disclosed in U.S. Pat. No. 4,885,155, issued December 5, 1989 to Parran & Sakkab; U.S. Pat. No. 3,678,154, issued July 18, 1972 to Widder et al.; U.S. Pat. No. 3,737,522, issued June 5, 1973 to Francis et al.; and U.S. Pat. No. 4,627,977, issued December 9, 1986 to Gaffer et al.; each is incorporated herein by reference. Suitable pyro ion sources include tetrasodium pyrophosphate, sodium acid pyrophosphate

($Na_2H_2P_2O_7$), tetrapotassium pyrophosphate ($K_4P_2O_7$); phosphates including, but not limited to, linear condensed polyphosphates of the general formula: $M_{(n+2)}P_nO_{(3n+1)}$ wherein M is Na or K, and n is an integer from 2 to 21; phosphonates and diphosphonates, such as EHDP (ethane-1-hydroxy-1,1-diphosphonate) and AHP (azacycloheptane-2,2-diphosphonic acid); pharmaceutically-acceptable alkali metal salts of pyrophosphates, polyphosphates, phosphonates and diphosphonates; and mixtures of any of the above. Preferred pyro ions are pyrophosphate ions; preferred polyphosphate ions are those of the above formula wherein n is 6, 13, and 21. Preferred alkali metals are sodium and potassium for solubility reasons; mixtures of alkali metal salts are acceptable.

The pH of oral compositions of the subject invention is critical but can be varied to some extent. Preferably the oral compositions are at a pH of from about 6 to about 9, more preferably from about 6.25 to about 8.75, more preferably still from about 7.5 to about 8.5.

During manufacture of a composition of this invention, the conditions for addition of each component should be optimized such that the pH of the mixture does not drop below formulation pH at any time during mixing the indredients.

Compositions

By "safe and effective amount" as used herein is meant an amount of compound or composition sufficient to induce a significant positive modification in the condition to be treated, but low enough to avoid serious side effects (at a reasonable benefit/risk ratio), within the scope of sound medical judgment. The safe and effective amount of the compound or composition will vary with the particular condition being treated, the age and physical condition of the patient being treated, the severity of the condition, the duration of the treatment, the nature of concurrent therapy, the specific compound or composition employed, the particular pharmaceutically-acceptable carrier utilized, and like factors.

By the term "comprising", as used herein, is meant that various additional components can be conjointly employed in the compositions of this invention.

Components of the topical, oral carrier are suitable for administration to the oral cavity of a human or lower animal and are compatible with one another and the other components, especially with the Actives, used in an oral composition of the subject invention. The term "compatible" as used herein, means that the components are capable of being co-mingled with one another, in a manner such that there is no interaction which would substantially reduce the efficacy of the oral composition under ordinary use conditions.

Preferred topical, oral carriers provide the desired characteristics for mouthwashes, mouth rinses, mouth sprays, dental treatment solutions, toothpastes, dental gels, toothpowders, prophylaxis pastes, lozenges, chewing gums, and the like. The topical, oral carriers of the subject invention comprise components typically used in such compositions which are well known to a skilled practitioner. Such components include, but are not limited to, anticaries agents, antiplaque agents, anticalculus agents, dental abrasives, surfactants, flavoring agents, sweetening agents, binders, humectants, thickening agents, buffering agents, preservatives, coloring agents and pigments, ethanol and water.

Water is an optional component of the topical, oral carriers of the compositions of the subject invention. Water employed in the preparation of the commercially suitable compositions should preferably be of low ion content and free of organic impurities. Water preferably comprises from about 2% to about 99%, more preferably from about 20% to about 95% of the compositions of the subject invention. When in the form of toothpaste, the compositions preferably comprise from about 2% to about 80%, more preferably from about 30% to about 60%, water, while mouthwashes comprise preferably from about 45% to about 99%, more preferably from about 75% to about 98%, water.

Dental abrasives useful in the topical, oral carriers of the compositions of the subject invention include many different materials. The material selected must be one which is compatible with the composition of interest and does not excessively abrade dentin. These include, for example, silicas, including gels and precipitates, calcium carbonate, dicalcium orthophosphate dihydrate, calcium

pyrophosphate, tricalcium phosphate, calcium polymeta-phosphate, insoluble sodium polymeta-phosphate, hydrated alumina, and resinous abrasive materials such as particulate condensation products of urea and formaldehyde, and other materials such as those disclosed by Cooley et al. in U.S. Pat. No. 3,070,510, issued December 25, 1962, incorporated herein by reference. Mixtures of abrasives may also be used.

Silica dental abrasives, of various types, can provide the unique benefits of exceptional dental cleaning and polishing performance without unduly abrading tooth enamel or dentin. For this reason they are preferred for use herein.

The silica abrasive polishing materials useful herein, as well as the other abrasives, generally have an average particle size ranging between about 0.1 and 30 microns, preferably between about 5 and 15 microns. The silica abrasive can be precipitated silica or silica gels such as the silica xerogels described in U.S. Pat. No. 3,538,230, issued March 2, 1970 to Pader et al., and in U.S. Pat. No. 3,862,307, issued June 21, 1975 to DiGiulio, both incorporated herein by reference. Preferred are the silica xerogels marketed under the tradename Syloid® by the W.R. Grace & Company, Davidson Chemical Division. Preferred precipitated silica materials include those marketed by the J. M. Huber Corporation under the tradename, Zeodent®, particularly the silica carrying the designation Zeodent 119®. These silica abrasives are described in U.S. Pat. No. 4,340,583, Wason, issued July 20, 1982, incorporated herein by reference.

Mixtures of abrasives may be used. The amount of abrasive in the compositions described herein ranges from about 6% to about 70%, preferably from about 15% to about 50%, when the dentifrice is a toothpaste. Higher levels, as high as 90%, may be used if the composition is a tooth powder.

Flavoring agents can also be added to the oral compositions of the subject invention to make them more palatable. Suitable flavoring agents include menthol, oil of wintergreen, oil of peppermint, oil of spearmint, oil of sassafras, and oil of clove. Flavoring agents are

generally included in the subject compositions in amounts of from 0% to about 3%, preferably from about 0.04% to about 2% by weight.

Coloring agents may be added to compositions of the subject invention to improve appearance. If present, coloring agents typically are included at levels of from about 0.001% to about 0.5% by weight.

Sweetening agents are also preferred in the compositions of the subject invention to make them more palatable. Sweetening agents which can be used include aspartame, acesulfame, saccharin salts, dextrose, glucose, levulose thaumatin, D-tryptophan, dihydrochalcones, and cyclamate salts. Saccharin salts are preferred. Sweetening agents are generally used in the subject compositions in amounts of from 0% to about 6%, preferably from about 0.005% to about 5% by weight.

Oral compositions can also contain a surfactant. Suitable surfactants are those which are reasonably stable and form suds throughout a wide pH range, including nonsoap anionic, nonionic, cationic, zwitterionic and amphoteric organic synthetic detergents, and compatible mixtures thereof. Many of these suitable surfactants are disclosed in U.S. Pat. No. 4,051,234, issued to Gieske et al. on September 27, 1977, and in U.S. Pat. No. 3,959,458 issued to Agricola, Briner, Granger and Widder on May 25, 1976, both of which are incorporated herein by reference. Surfactants are typically present in compositions of the subject invention at a level of from 0% to about 20%, preferably from about 0.1, more preferably from about 1% to about 4% by weight. Surfactants may also be used as solubilizing agents to help retain sparingly soluble components, e.g., some flavoring agents, in solutions. Surfactants suitable for this purpose include polysorbates and poloxamers. Preferred are surfactants which are non-ionic at the formulation pH of the compositions.

In preparing oral compositions of the subject invention, it is desirable to add binders and/or thickening agents, particularly to toothpaste compositions to provide a desired consistency. Suitable binders for these compositions are natural gums such as gum karaya, gum arabic, and gum tragacanth; polysaccharide gums such as xanthan gum; and other natural products such as carrageenan;

chemically modified natural products such as those based on cellulose esters, that is, carboxylmethylcellulose (CMC), hydroxyethylcellulose (HEC), and hydroxypropylcellulose (HPC); and synthetic binders such as polyvinylpyrrolidone; and water soluble salts of cellulose ethers such as sodium carboxymethyl cellulose and sodium carboxymethyl hydroxyethyl cellulose. Carboxyvinyl polymer binders are less desirable, but may be used. Colloidal magnesium aluminum silicate or finely divided silica can be used as part of the thickening agent to further improve texture. Blends and mixtures of the suitable binders may significantly improve the characteristics of compositions made therewith. Preferred binders are chemically modified celluloses such as CMC or HEC; more preferred is HEC. Binders and thickening agents are generally present in the compositions of the subject invention in amounts of from about 0.1% to 10%, preferably from about 0.25% to about 7.5%, more preferably from about 0.5% to about 3.5%.

Another optional component of the oral carriers of the compositions of the subject invention is a humectant. The humectant serves to keep toothpaste compositions from hardening upon exposure to air, and to give mouthwash and toothpaste compositions a moist feel to the mouth. Certain humectants can also impart desirable sweetness of flavor to mouthwash and toothpaste compositions. The humectant, on a pure humectant basis, generally comprises from 0% to about 70%, preferably from about 2% to about 55%, by weight of the compositions herein. Suitable humectants for use in compositions of the subject invention include edible polyhydric alcohols such as glycerin, sorbitol, xylitol, polyethylene glycol, and propylene glycol, especially sorbitol and glycerin.

Opacifiers may also be used in toothpastes of the subject invention to render the toothpaste opaque. Suitable opacifiers include titanium dioxide and some abrasives including, for example, magnesium aluminum silicate. Opacifiers generally comprise from 0% to about 4%, preferably from about 0.5% to about 3% by weight of the compositions herein.

Other optional components of the compositions of the subject invention are preservatives. The preservatives prevent microbial growth in the compositions. Suitable preservatives include

methylparaben, propylparaben, benzoates and ethanol. If the preservative is ethanol, it generally comprises from 0% to about 35% by weight, preferably from about 5% to about 15%, of the compositions herein. Other preservatives generally comprise from 0% to about 5% by weight, preferably from about 0.1% to about 2%, of the compositions herein.

Antimicrobial, antiplaque agents can also optionally be present in the oral compositions of the subject invention, on the condition that they are compatible with the Actives. Such agents may include, but are not limited to, triclosan, 2,4,4'-trichloro-2'-hydroxydiphenyl ether, as described The Merck Index, 11th Ed. (1989), p. 1520 (entry No. 9573); chlorhexidine, (Merck Index, No. 2090); alexidine (Merck Index, No. 222); hexetidine (Merck Index, No. 4624); sanguinarine (Merck Index, No. 8320); benzalkonium chloride (Merck Index, No. 1066); salicylanilide (Merck Index, No. 8299); domiphen bromide (Merck Index, No. 3411); cetylpyridinium chloride, (CPC) (Merck Index, No. 2024); tetradecylpyridinium chloride, (TPC); N-tetradecyl-4-ethylpyridinium chloride (TDEPC); octenidine; delmopinol, octapinol, and other piperidino derivatives; nicin preparations; antibiotics such as augmentin, amoxicillin, tetracycline, doxycycline, minocycline, and metronidazole; and peroxides, such as cylium peroxide, hydrogen peroxide, and magnesium monoperthalate and its analogs as described in U.S. Patent No. 4,670,252; and analogs and salts of the above antimicrobial antiplaque agents. If present, the antimicrobial antiplaque agents may comprise from 0% to about 6%, preferably from about 0.1% to about 5% by weight of the compositions of the subject invention.

Bleaching agents can also be present in the oral compositions of the subject invention. Suitable bleaching agents include organic and inorganic oxidizing agents such as hydrogen peroxide, alkali metal peroxides and superoxide and organic peroxides such as monoper-oxyphthalates and perbenzoic derivatives. If present, such bleaching agents may comprise from 0% to about 6%, preferably from about 1% to about 5% by weight of the compositions of the subject invention.

Nutrients can also be present in the oral composition of the subject invention, on condition that they are compatible with the Actives. Such agents may include folate, retinoids (Vitamin A), Vitamin C, Vitamin E. If present, the nutrients generally comprise from about 0.001% to about 10% by weight of the compositions of the subject invention.

Other optional ingredients include a safe and effective amount of a fluoride ion source, which typically is in the form of a water-soluble fluoride compound. This water-soluble fluoride compound is typically present in the compositions of the subject invention in an amount sufficient to give a fluoride concentration of from about 0.0025% to about 5.0% by weight, preferably from about 0.005% to about 2.0% by weight. Preferred fluoride sources are sodium fluoride, acidulated phosphate fluoride, and sodium monofluorophosphate. U.S. Pat. No. 3,678,154, issued July 18, 1972 to Widder et al., discloses such salts as well as others, and is incorporated herein by reference.

Preferred compositions of the subject invention are in the form of dentifrices, especially toothpastes. Components of toothpastes generally include a dental abrasive (from about 10% to about 50%), a surfactant (from about 0.5% to about 10%), a thickening agent (from about 0.1% to about 5%), a humectant (from about 10% to about 55%), a flavoring agent (from about 0.04% to about 2%), a sweetening agent (from about 0.1% to about 3%), a coloring agent (from about 0.01% to about 0.5%) and water (from about 2% to about 45%).

Other preferred compositions of the subject invention are mouth rinses, mouthwashes and mouth sprays. Components of such mouthwashes and mouth sprays include water (from about 45% to about 95%), ethanol (from 0% to about 25%), humectant (from 0% to about 50%), surfactant (from about 0.01% to about 7%), flavoring agent (from about 0.04% to about 2%), sweetening agent (from about 0.1% to about 3%), and coloring agent (from about 0.001% to about 0.5%). Such mouth rinses, mouthwashes and mouth sprays may also include an antiplaque agent (from about 0.1% to about 5%).

Other preferred compositions of the present invention are dental solutions. Components of such dental solutions generally include

water (from about 90% to about 99%), preservative (from about 0.01% to about 0.5%), thickening agent (from 0% to about 5%), flavoring agent (from about 0.04% to about 2%), sweetening agent (from about 0.1% to about 3%), and surfactant (from 0% to about 5%).

Methods of Use

Another aspect of the subject invention involves methods of treating or preventing mouth odor, dental plaque, calculus and gingivitis, by application of compositions comprising a safe and effective amount of Actives, to tissues of the oral cavity. Such compositions are described hereinabove.

These methods involve administering a safe and effective amount of Actives, typically by administering an oral composition of the subject invention, as described hereinabove, to the oral cavity. Generally an amount of composition comprising at least about 0.001g of the Actives is effective. The teeth and other oral cavity tissues are exposed to the Actives.

When the oral composition is a toothpaste, typically from about 0.3 grams to about 15 grams, preferably from about 0.5 grams to about 5 grams, more preferably from about 1 to about 2 grams, of toothpaste is applied to an applicating device e.g., a toothbrush. The applicating device is then contacted with the oral cavity surfaces in a manner such that the oral composition is contacted with tissue of the oral cavity, especially the teeth and gums. The applicating device may be further used to effect an even distribution of the oral composition to the tooth surface, for example by brushing. The application preferably lasts for a period of from about 15 seconds to about 10 minutes, more preferably from about 30 seconds to about 3 minutes, more preferably still from about 1 minute to about 2 minutes. Following application, the toothpaste residue is typically removed from the tooth surface by using a liquid acceptable to the oral cavity, typically water, to rinse and be expectorated from the oral cavity.

When the oral composition is a mouthwash, typically from about 1 ml. to about 20 ml., preferably from about 2 ml. to about 15 ml., most preferably from about 10 ml. to about 15 ml., of liquid mouthwash containing the antiplaque Active is introduced to the oral cavity. The liquid mouthwash is then agitated for from about 10 seconds to about

10 min., preferably from about 15 seconds to about 3 min., more preferably from about 30 seconds to about 2 minutes, within the oral cavity to obtain an improved distribution of the mouthwash over the tissue of the oral cavity. Following agitation, the mouthwash is typically expectorated from the oral cavity.

Application frequency is preferably from about 3 times weekly to about 4 times daily, more preferably from about once daily to about 3 times daily, more preferably still from about once to about twice daily. The period of such treatment typically ranges from about one day to a lifetime.

Oral Composition Examples

The following non-limiting examples further describe and demonstrate preferred embodiments within the scope of the subject invention. The examples are given solely for illustration and are not to be construed as limitations of the subject invention as many variations are possible without departing from the spirit and scope of the subject invention.

The compositions of the subject invention can be made using methods which are commonly used to produce oral care products.

EXAMPLES I-XI

The following are examples of dentifrice compositions of the subject invention and are made using conventional processes. The numbers listed are weight percentages of the compositions. During manufacture of each composition, a minimum pH of 7.5 is maintained.

Components	Ex. I	Ex. II	Ex. III	Ex. IV	Ex. V	Ex. VI
Sorbitol	21.17	21.17	14.2	18.3	21.17	31.65
PEG-6	3	3	3	3	3	
Citric Acid	0.69	0.34	0.51	0.51	1.03	1.46
Sodium Citrate	4.84	2.42	3.63	3.63	7.25	3.68
Zinc Nitrate						2.97
Zinc Sulfate				1.61		
Zinc Chloride	1.36				1.36	
Zinc Oxide		0.81	0.81			

Tetrapotassium Pyrophosphate (60% aqueous solution)	5.08	12.71	10.16	7.62	2.54	11.87
Sodium Acid Pyrophosphate	1.33	3.32	2.65	1.99	0.66	
Tetrasodium Pyrophosphate	1.28	3.19	2.55	1.91	0.64	
Sodium Fluoride	0.24	0.24	0.24	0.24	0.24	0.24
Sodium Saccharin	0.46	0.46	0.46	0.46	0.46	0.46
Titanium Dioxide	0.5	0.5	0.5	0.5	0.5	0.5
Silica	22	22	22	22	22	22
Glycerin	9	9	9	9	9	9
Carboxymethylcellulose	1	1	0.75		0.75	0.75
Xanthan Gum			0.75	0.75	0.75	0.75
Hydroxyethylcellulose				0.75		
Sodium Lauryl Sulfate (27.9% Aqueous solution)	4	4	4	4	4	4
Flavor	1.1	1.1	1.1	1.1	1.1	1.1
Water	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
TOTAL	**100**	**100**	**100**	**100**	**100**	**100**

Slurry pH: 7.1 to 7.3

Component	Ex. VII	Ex. VIII	Ex. IX	Ex. X	Ex. XI
Sorbitol	31.65	31.65	14.2	31.65	31.65
PEG-6	3	3	3	3	3
Citric Acid(anhydrous or monohydate)	1.44	0.91	0.73	0.88	2.94
Sodium Citrate	3.23	0.144	4.62		
Zinc Oxide	0.81	0.407	0.81	0.374	0.13
Tetrapotassium Pyrophosphate (60% aqueous solution)	3.3		5.09	25.33	4.22
Sodium Acid Pyrophosphate			1.28		

Tetrasodium Pyrophosphate	2.66	6.65	1.33		
Sodium Fluoride	0.24	0.24	0.24	0.24	0.24
Sodium Saccharin	0.46	0.46	0.25	0.25	0.46
Titanium Dioxide	0.5	0.5	0.5	0.5	0.5
Silica	22	22	22	22	22
Glycerin	2.25	2.25	8	2.25	2.25
Carboxymethylcellulose	0.5	0.5	0.75		0.75
Xanthan Gum	0.4	0.4	0.75	0.75	0.75
Hydroxyethylcellulose				0.75	
Sodium Lauryl Sulfate (27.9% Aqueous solution)	4	4	4	4	4
Flavor	1.1	1.1	1	1	1
KOH/HCl and Water	q.s. to pH 7.5	q.s. to pH 8.0	q.s. to pH 8.0	q.s. to pH 8.0	q.s. to pH 8.5
Total	100	100	100	100	100

Slurry pH: 7.5 to 8.5

EXAMPLES XII-XVI

The following are examples of mouthwash and dental rinse compositions of the subject invention and are made using conventinal processes. The amounts listed are weight percentages of the compositions. During manufacture, the pH of the following compositions is maintained at a minimum of pH 7.5.

Component	Ex. XII	Ex. XIII	Ex. XIV	Ex. XV	Ex. XVI
Glycerin	10	10	10	10	10
Ethanol	10	10	10	10	10
Sodium Citrate	0.41	3.84			1.28
Citric Acid			11.40	3.80	
Zinc Chloride		1.36			
Zinc Oxide	0.081		1.63	0.81	0.41

Tetrapotassium Pyrophosphate (60% Sol'n)	1.10			5.51	1.1
Tetrasodium Pyrophosphate				2.66	0.27
Sodium Tripolyphosphate			7.36		0.37
Sodium Acid Pyrophosphate		6.66			0.22
Sodium Lauryl Sulfate	0.4	0.4	0.4	0.4	0.4
Sodium Saccharin	0.03	0.03	0.03	0.03	0.03
Flavor	0.22	0.22	0.22	0.22	0.22
NaOH/HCL & Water	q.s. 100% at pH 7.5	q.s. 100% at pH 8.5	q.s. 100% at pH 8.5	q.s. 100% at pH 7.5	q.s. 100% at pH 8.0

While particular embodiments of the subject invention have been described, it will be obvious to those skilled in the art that various changes and modifications to the subject invention can be made without departing from the spirit and scope of the invention. It is intended to cover, in the appended claims, all such modifications that are within the scope of the subject invention.

Claims

1. A composition for treating or preventing dental plaque, calculus and gingivitis, or malodor of the oral cavity, comprising:

(a) (i) a source of a safe and effective amount of zinc ions; (ii) a source of citrate ions; and (iii) one or more anticalculus agents selected from pyrophosphate, phosphonate, diphosphonate and pharmaceutically-acceptable linear condensed poly-phosphates of the general formula: $(P_nO_{(3n+1)})^{(n+2)-}$ wherein n is an integer from 2 to 21;

wherein the molar ratio of zinc:citrate is at most 1:1; the molar ratio of zinc:pyro is at most 1:1; and

(b) a pharmaceutically-acceptable topical oral carrier.

2. The composition according to Claim 1 wherein the molar ratio of zinc ions:citrate ions is from 1:1 to 1:20, preferably from 1:1 to 1:5, more preferably from 1:1 to 1:4, and the molar ratio of zinc ions to the anticalculus agents is from 1:1 to 1:20, preferably from 1:1 to 1:8, more preferably from 1:1 to 1:5.

3. The composition according to any of Claims 1-2 wherein the composition is at a pH of from 6 to 9, preferably from 7.5 to 8.5 and the sum of the molar ratio amounts of citrate ions and anticalculus agents is from 3 to 9.

4. The composition of any of Claims 1-3 which is in the form of a dentifrice, preferably wherein the pharmaceutically-acceptable topical oral carrier comprises a dental abrasive.

5. The composition according to any of Claims 1-4 which comprises from 0.1% to 2%, preferably from 0.25% to 1%, by weight zinc ions.

6. A composition according to any of Claims 1-3 which is in the form of a mouth rinse, preferably wherein the pharmaceutically-acceptable topical oral carrier comprises a material selected from a humectant, ethanol, and a nonionic surfactant.

7. The composition according to any of Claims 1-3 and 6 comprising from 0.005% to 0.5% by weight zinc ions.

8. The composition according to any of Claims 1-7 wherein the anticalculus agent is selected from pyrophosphate, EHDP, AHP, and linear condensed polyphosphates of the general formula: $(P_nO_{(3n+1)})^{(n+2)-}$ wherein n is 6, 13, or 21, preferably the anticalc agent is pyrophosphate.

9. The composition according to any of Claims 1-8 which comprises a source of fluoride ions yielding from 0.0025% to 5% by weight fluoride ions.

10. A method for treating or preventing dental plaque, calculus or malador of the oral cavity comprising administering to the oral cavity of a human or lower mammal a safe and effective amount of a composition selected from Claims 1-9.

INTERNATIONAL SEARCH REPORT

Interna 1 Application No
PCT/US 93/11787

A. CLASSIFICATION OF SUBJECT MATTER
IPC 5 A61K7/16

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 5 A61K

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

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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X	RESEARCH DISCLOSURE no. 321 , January 1991 , EMSWORTH GB pages 80 - 81 'oral compositions' see paragraph 4; example 9	1-10
X	EP,A,0 295 116 (UNILEVER PLC.) 14 December 1988 see the whole document	1-10

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
6 April 1994	20. 04. 94

Name and mailing address of the ISA	Authorized officer
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INTERNATIONAL SEARCH REPORT

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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