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(54) Title: FLUORIDE-STABLE ZINC CONTAINING ORAL CARE COMPOSITIONS

(57) Abstract: Described herein are oral care compositions comprising a zinc ion source, a fluoride ion source, and a basic amino acid; along with methods of making and using the same.



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## FLUORIDE-STABLE ZINC CONTAINING COMPOSITIONS

### BACKGROUND

[0001] Dental erosion involves demineralization and damage to the tooth structure due to acid attack from nonbacterial sources. Erosion is found initially in the enamel and, if unchecked, may proceed to the underlying dentin. Dental erosion may be caused or exacerbated by acidic foods and drinks, exposure to chlorinated swimming pool water, and regurgitation of gastric acids. The tooth enamel is a negatively charged surface, which naturally tends to attract positively charged ions such as hydrogen and calcium ions, while resisting negatively charged ions such as fluoride ions. Depending upon relative pH of surrounding saliva, the tooth enamel will lose or gain positively charged ions such as calcium ions. Generally saliva has a pH between 7.2 and 7.4. When the pH is lowered and concentration of hydrogen ions becomes relatively high, the hydrogen ions will replace the calcium ions in the enamel, forming hydrogen phosphate (phosphoric acid), which damages the enamel and creates a porous, sponge-like roughened surface. If saliva remains acidic over an extended period, then remineralization may not occur, and the tooth will continue to lose minerals, causing the tooth to weaken and ultimately to lose structure.

[0002] There is a need for improved products for treating and reducing erosion.

[0003] Heavy metal ions, such as zinc, are resistant to acid attack. Zinc ranks above hydrogen in the electrochemical series, so that metallic zinc in an acidic solution will react to liberate hydrogen gas as the zinc passes into solution to form di-cations,  $Zn^{2+}$ . Zinc has been shown to have antibacterial properties in plaque and caries studies.

[0004] Soluble zinc salts, such as zinc citrate, have been used in dentifrice compositions, but have several disadvantages. Free zinc ions may react with fluoride ions to produce zinc fluoride, which is insoluble and so reduces the availability of both the zinc and the fluoride. Moreover, zinc ions in solution impart an unpleasant, astringent mouthfeel, so formulations that provide effective levels of zinc, and also have acceptable organoleptic properties, have been difficult to achieve. Finally, the zinc ions will react with anionic surfactants such as sodium lauryl sulfate, thus interfering with foaming and cleaning.

### SUMMARY

[0005] It has now been discovered that formulations comprising zinc ions together with fluoride have enhanced fluoride stability when placed in combination with a basic amino acid, for example arginine or lysine. The basic amino acid appears to inhibit the formation of insoluble zinc fluoride, thereby enhancing the availability of both the zinc and fluoride. The available zinc aids in protecting against erosion, reducing bacterial colonization and biofilm development, and providing enhanced shine to the teeth, while the fluoride aids in strengthening the enamel and reducing cavity formation. The formulations, moreover, do not have the poor taste and mouthfeel and poor foaming and cleaning associated with conventional zinc-based oral care products.

[0006] The invention thus provides oral care compositions, for example dentifrices, that comprise a zinc ion source, a fluoride ion source, and a basic amino acid. The compositions may optionally further comprise a phosphate source. The compositions may be formulated in a conventional dentifrice or mouthwash base, e.g., comprising abrasives, e.g., silica abrasives, surfactants, foaming agents, vitamins, polymers, enzymes, humectants, thickeners, antimicrobial agents, preservatives, flavorings, colorings, and/or combinations thereof. For example, in one embodiment, the invention provides a dentifrice comprising ca. 1% zinc citrate, ca. 5% arginine, ca. 5% alkali phosphate salts, and ca. 1450ppm fluoride, in a silica abrasive dentifrice base.

[0007] The invention further provides methods of using the compositions of the invention to reduce and inhibit acid erosion of the enamel, clean the teeth, reduce bacterially-generated biofilm and plaque, reduce gingivitis, inhibit tooth decay and formation of cavities, and reduce dentinal hypersensitivity, comprising brushing the teeth with a composition of the invention.

[0008] Further areas of applicability of the present invention will become apparent from the detailed description provided hereinafter. It should be understood that the detailed description and specific examples, while indicating the preferred embodiment of the invention, are intended for purposes of illustration only and are not intended to limit the scope of the invention.

### DETAILED DESCRIPTION

[0009] The following description of the preferred embodiment(s) is merely exemplary in nature and is in no way intended to limit the invention, its application, or uses.

[0010] The invention therefore provides, in a first embodiment, an oral care composition, e.g., a mouthwash or a dentifrice, comprising a zinc ion source, a fluoride ion source, and a basic amino acid (Composition 1), e.g.,

- 1.1. Composition 1 wherein the zinc ion source is selected from zinc citrate, zinc sulfate, zinc silicate, zinc lactate, zinc phosphate, zinc oxide, and combinations thereof, e.g., in an effective amount, e.g., providing an amount of zinc effective inhibit erosion, e.g., from 0.005-5% zinc, e.g., 0.01 – 0.05% for a mouthwash or 0.1 to 3% for a dentifrice, e.g., a dentifrice comprising 1-3% zinc citrate.
- 1.2. Composition 1 in the form of a dentifrice further comprising an abrasive, e.g., an effective amount of a silica abrasive, e.g., 10-30%, e.g., about 20%.
- 1.3. Composition 1 in the form of a mouthwash.
- 1.4. Any of the foregoing compositions wherein the fluoride is in an amount effective inhibit tooth decay, e.g., 500 to 3000 ppm fluoride.
- 1.5. Any of the foregoing compositions wherein the fluoride is a salt selected from stannous fluoride, sodium fluoride, potassium fluoride, sodium monofluorophosphate, sodium fluorosilicate, ammonium fluorosilicate, amine fluoride (e.g., N'-octadecyltrimethylendiamine-N,N,N'- tris(2-ethanol)-dihydrofluoride), ammonium fluoride, titanium fluoride, hexafluorosulfate, and combinations thereof.
- 1.6. Any of the foregoing compositions wherein the basic amino acid is present in an amount sufficient to inhibit the formation of zinc fluoride precipitate, e.g. about 0.5 wt. % to about 20 wt. % of the total composition weight, about 0.5 wt. % to about 10 wt. % of the total composition weight, for example about 1.5 wt. %, about 3.75 wt. %, about 5 wt. %, or about 7.5 wt. % of the total composition weight in the case of a dentifrice, or for example about 0.5-2 wt. %, e.g., about 1% in the case of a mouthwash.
- 1.7. Any of the foregoing compositions wherein the basic amino acid is selected f
- 1.8. Any of the preceding compositions wherein the basic amino acid is present in an amount sufficient to raise the pH of the formulation to greater than pH 8, e.g., to pH 8.5-10, e.g., about pH 9-9.5

- 1.9. Any of the preceding compositions comprising an effective amount of one or more alkali phosphate salts, e.g., sodium, potassium or calcium salts, e.g., selected from alkali dibasic phosphate and alkali pyrophosphate salts, e.g., alkali phosphate salts selected from sodium phosphate dibasic, potassium phosphate dibasic, dicalcium phosphate dihydrate, calcium pyrophosphate, tetrasodium pyrophosphate, tetrapotassium pyrophosphate, sodium tripolyphosphate, and mixtures of any of two or more of these, e.g., in an amount of 1-20%, e.g., 2-8%, e.g., ca. 5%, by weight of the composition.
- 1.10. Any of the foregoing compositions comprising buffering agents, e.g., sodium phosphate buffer (e.g., sodium phosphate monobasic and disodium phosphate).
- 1.11. Any of the foregoing compositions comprising a humectant, e.g., selected from glycerin, sorbitol, propylene glycol, polyethylene glycol, xylitol, and mixtures thereof, e.g. comprising at least 20%, e.g., 20-40%, e.g., 25-35% glycerin.
- 1.12. Any of the preceding compositions comprising one or more surfactants, e.g., selected from anionic, cationic, zwitterionic, and nonionic surfactants, and mixtures thereof, e.g., comprising an anionic surfactant, e.g., a surfactant selected from sodium lauryl sulfate, sodium ether lauryl sulfate, and mixtures thereof, e.g. in an amount of from about 0.3% to about 4.5% by weight, e.g. 1-2% sodium lauryl sulfate (SLS); and/or a zwitterionic surfactant, for example a betaine surfactant, for example cocamidopropylbetaine, e.g. in an amount of from about 0.1% to about 4.5% by weight, e.g. 0.5-2% cocamidopropylbetaine.
- 1.13. Any of the preceding compositions further comprising a viscosity modifying amount of one or more of polysaccharide gums, for example xanthan gum or carrageenan, silica thickener, and combinations thereof.
- 1.14. Any of the preceding compositions comprising gum strips or fragments.
- 1.15. Any of the preceding compositions further comprising flavoring, fragrance and/or coloring.
- 1.16. Any of the foregoing compositions comprising an effective amount of one or more antibacterial agents, for example comprising an antibacterial agent selected from halogenated diphenyl ether (e.g. triclosan), herbal extracts and essential oils (e.g., rosemary extract, tea extract, magnolia extract, thymol, menthol, eucalyptol,

geraniol, carvacrol, citral, hinokitol, catechol, methyl salicylate, epigallocatechin gallate, epigallocatechin, gallic acid, miswak extract, sea-buckthorn extract), bisguanide antiseptics (e.g., chlorhexidine, alexidine or octenidine), quaternary ammonium compounds (e.g., cetylpyridinium chloride (CPC), benzalkonium chloride, tetradecylpyridinium chloride (TPC), N-tetradecyl-4-ethylpyridinium chloride (TDEPC)), phenolic antiseptics, hexetidine, octenidine, sanguinarine, povidone iodine, delmopinol, salifluor, metal ions (e.g., zinc salts, for example, zinc citrate, stannous salts, copper salts, iron salts), sanguinarine, propolis and oxygenating agents (e.g., hydrogen peroxide, buffered sodium peroxyborate or peroxycarbonate), phthalic acid and its salts, monoperthalic acid and its salts and esters, ascorbyl stearate, oleoyl sarcosine, alkyl sulfate, dioctyl sulfosuccinate, salicylanilide, domiphen bromide, delmopinol, octapinol and other piperidino derivatives, nicin preparations, chlorite salts; and mixtures of any of the foregoing; e.g., comprising triclosan or cetylpyridinium chloride.

- 1.17. Any of the foregoing compositions comprising an antibacterially effective amount of triclosan, e.g. 0.1 -0.5%, e.g. about 0.3%.
- 1.18. Any of the preceding compositions further comprising a whitening agent, e.g., a selected from the group consisting of peroxides, metal chlorites, perborates, percarbonates, peroxyacids, hypochlorites, and combinations thereof.
- 1.19. Any of the preceding compositions further comprising hydrogen peroxide or a hydrogen peroxide source, e.g., urea peroxide or a peroxide salt or complex (e.g., such as peroxyphosphate, peroxycarbonate, perborate, peroxysilicate, or persulphate salts; for example calcium peroxyphosphate, sodium perborate, sodium carbonate peroxide, sodium peroxyphosphate, and potassium persulfate);
- 1.20. Any of the preceding compositions further comprising an agent that interferes with or prevents bacterial attachment, e.g., solbrol or chitosan.
- 1.21. Any of the preceding compositions further comprising a source of calcium and phosphate selected from (i) calcium-glass complexes, e.g., calcium sodium phosphosilicates, and (ii) calcium-protein complexes, e.g., casein phosphopeptide-amorphous calcium phosphate

- 1.22. Any of the preceding compositions further comprising a soluble calcium salt, e.g., selected from calcium sulfate, calcium chloride, calcium nitrate, calcium acetate, calcium lactate, and combinations thereof.
- 1.23. Any of the preceding compositions further comprising a physiologically or orally acceptable potassium salt, e.g., potassium nitrate or potassium chloride, in an amount effective to reduce dentinal sensitivity.
- 1.24. Any of the foregoing compositions further comprising an anionic polymer, e.g., a synthetic anionic polymeric polycarboxylate, e.g., wherein the anionic polymer is selected from 1:4 to 4:1 copolymers of maleic anhydride or acid with another polymerizable ethylenically unsaturated monomer; e.g., wherein the anionic polymer is a methyl vinyl ether/maleic anhydride (PVM/MA) copolymer having an average molecular weight (M.W.) of about 30,000 to about 1,000,000, e.g. about 300,000 to about 800,000, e.g., wherein the anionic polymer is about 1-5%, e.g., about 2%, of the weight of the composition.
- 1.25. Any of the preceding compositions further comprising a breath freshener, fragrance or flavoring.
- 1.26. Any of the foregoing compositions, wherein the pH of the composition is either acidic or basic, e.g., from pH 4 to pH 5.5 or from pH 8 to pH 10.
- 1.27. Any of the foregoing compositions which is a dentifrice, wherein the composition comprises
  - 0.5-2.5%, e.g. about 1% or about 2% zinc citrate;
  - 1-10%, e.g., ca. 5% L-arginine (free base);
  - 2-8%, e.g., ca. 5% alkali phosphate salts, e.g., selected from sodium phosphate dibasic, potassium phosphate dibasic, dicalcium phosphate dihydrate, calcium pyrophosphate, tetrasodium pyrophosphate, tetrapotassium pyrophosphate, sodium tripolyphosphate, and mixtures of any of two or more of these.
  - 700-2000 ppm, e.g., ca. 1450ppm fluoride, e.g., 0.3-0.4%, e.g., ca. 0.32% sodium fluoride;in a silica abrasive dentifrice base.

- 1.28. Any of the foregoing compositions comprising substantially the same ingredients as in the test formulation A or B in Example 1 below, e.g comprising the listed ingredients in amounts in a range of +/- 5% of the listed amounts.
- 1.29. Any of the preceding compositions effective upon application to the oral cavity, e.g., with brushing, to (i) reduce hypersensitivity of the teeth, (ii) to reduce plaque accumulation, (iii) reduce or inhibit demineralization and promote remineralization of the teeth, (iv) inhibit microbial biofilm formation in the oral cavity, (v) reduce or inhibit gingivitis, (vi) promote healing of sores or cuts in the mouth, (vii) reduce levels of acid producing bacteria, (viii) to increase relative levels of non-cariogenic and/or non-plaque forming bacteria, (ix) reduce or inhibit formation of dental caries, (x), reduce, repair or inhibit pre-carious lesions of the enamel, e.g., as detected by quantitative light-induced fluorescence (QLF) or electrical caries measurement (ECM), (xi) treat, relieve or reduce dry mouth, (xii) clean the teeth and oral cavity, (xiii) reduce erosion, (xiv) whiten teeth; and/or (xv) promote systemic health, including cardiovascular health, e.g., by reducing potential for systemic infection via the oral tissues.
- 1.30. A composition obtained or obtainable by combining the ingredients as set forth in any of the preceding compositions.

**[0011]** The invention further provides the use of a basic amino acid, e.g., arginine, to enhance fluoride delivery in an oral care composition, e.g., a dentifrice, comprising a zinc ion source and a fluoride ion source.

**[0012]** The invention further provides methods of using the compositions of the invention, to increase zinc levels in the enamel and to treat, reduce or control the incidence of enamel erosion, comprising applying a composition as described above, e.g., any of Composition 1, et seq., to the teeth, e.g., by brushing. In various embodiments, the invention provides to (i) reduce hypersensitivity of the teeth, (ii) to reduce plaque accumulation, (iii) reduce or inhibit demineralization and promote remineralization of the teeth, (iv) inhibit microbial biofilm formation in the oral cavity, (v) reduce or inhibit gingivitis, (vi) promote healing of sores or cuts in the mouth, (vii) reduce levels of acid producing bacteria, (viii) to increase relative levels of non-cariogenic and/or non-plaque forming bacteria, (ix) reduce or inhibit formation of dental



caries, (x), reduce, repair or inhibit pre-carious lesions of the enamel, e.g., as detected by quantitative light-induced fluorescence (QLF) or electrical caries measurement (ECM), (xi) treat, relieve or reduce dry mouth, (xii) clean the teeth and oral cavity, (xiii) reduce erosion, (xiv) whiten teeth; (xv) reduce tartar build-up, and/or (xvi) promote systemic health, including cardiovascular health, e.g., by reducing potential for systemic infection via the oral tissues, comprising applying any of Compositions 1, et seq. as described above to the oral cavity of a person in need thereof, e.g., by brushing the teeth one or more times per day with any of Compositions 1, et seq. The invention further provides Compositions 1, et seq. for use in any of these methods.

**[0013] Active Agents:** The compositions of the invention may comprise various agents which are active to protect and enhance the strength and integrity of the enamel and tooth structure and/or to reduce bacteria and associated tooth decay and/or gum disease. Effective concentration of the active ingredients used herein will depend on the particular agent and the delivery system used. It is understood that a toothpaste for example will typically be diluted with water upon use, while a mouth rinse typically will not be. Thus, an effective concentration of active in a toothpaste will ordinarily be 5-15x higher than required for a mouth rinse. The concentration will also depend on the exact salt or polymer selected. For example, where the active agent is provided in salt form, the counterion will affect the weight of the salt, so that if the counterion is heavier, more salt by weight will be required to provide the same concentration of active ion in the final product. Arginine, where present, may be present at levels from, e.g., about 0.1 to about 20 wt % (expressed as weight of free base), e.g., about 1 to about 10 wt % for a consumer toothpaste or about 7 to about 20 wt % for a professional or prescription treatment product. Fluoride where present may be present at levels of, e.g., about 25 to about 25,000 ppm, for example about 750 to about 2,000 ppm for a consumer toothpaste, or about 2,000 to about 25,000 ppm for a professional or prescription treatment product. Levels of antibacterial agents will vary similarly, with levels used in toothpaste being e.g., about 5 to about 15 times greater than used in mouthrinse. For example, a triclosan toothpaste may contain about 0.3 wt % triclosan.

**[0014] Fluoride Ion Source:** The oral care compositions may further include one or more fluoride ion sources, e.g., soluble fluoride salts. A wide variety of fluoride ion-yielding materials can be employed as sources of soluble fluoride in the present compositions. Examples of

suitable fluoride ion-yielding materials are found in U.S. Pat. No. 3,535,421, to Briner et al.; U.S. Pat. No. 4,885,155, to Parran, Jr. et al. and U.S. Pat. No. 3,678,154, to Widder et al. Representative fluoride ion sources include, but are not limited to, stannous fluoride, sodium fluoride, potassium fluoride, sodium monofluorophosphate, sodium fluorosilicate, ammonium fluorosilicate, amine fluoride, ammonium fluoride, and combinations thereof. In certain embodiments the fluoride ion source includes stannous fluoride, sodium fluoride, sodium monofluorophosphate as well as mixtures thereof. In certain embodiments, the oral care composition of the invention may also contain a source of fluoride ions or fluorine-providing ingredient in amounts sufficient to supply about 25 ppm to about 25,000 ppm of fluoride ions, generally at least about 500 ppm, e.g., about 500 to about 2000 ppm, e.g., about 1000 to about 1600 ppm, e.g., about 1450 ppm. The appropriate level of fluoride will depend on the particular application. A toothpaste for general consumer use would typically have about 1000 to about 1500 ppm, with pediatric toothpaste having somewhat less. A dentifrice or coating for professional application could have as much as about 5,000 or even about 25,000 ppm fluoride. Fluoride ion sources may be added to the compositions of the invention at a level of about 0.01 wt. % to about 10 wt. %; in some embodiments, from about 0.1 wt% to about 1.2 wt%; in other embodiments from about 0.3 wt. % to about 1 wt. %, and in another embodiment about 0.5 wt. % to about 0.8 wt. % by weight of the composition in another embodiment. Weights of fluoride salts to provide the appropriate level of fluoride ion will obviously vary based on the weight of the counterion in the salt.

**[0015]** Amino acids: In some embodiments, the compositions of the invention comprise an amino acid. In particular embodiments, the amino acid may be a basic amino acid. By “basic amino acid” is meant the naturally occurring basic amino acids, such as arginine, lysine, and histidine, as well as any basic amino acid having a carboxyl group and an amino group in the molecule, which is water-soluble and provides an aqueous solution with a pH of about 7 or greater. Accordingly, basic amino acids include, but are not limited to, arginine, lysine, citrulline, ornithine, creatine, histidine, diaminobutanoic acid, diaminopropionic acid, salts thereof or combinations thereof. In a particular embodiment, the basic amino acids are selected from arginine, citrulline, and ornithine. In certain embodiments, the basic amino acid is arginine, for example, l-arginine, or a salt thereof. In other embodiments, the amino acid is quaternized,

i.e., the amino group is additionally substituted to form a quaternary ammonium moiety, which may form an inner salt with the carboxyl group, for example, betaine (*N,N,N*-trimethylglycine).

**[0016]** In various embodiments, the amino acid is present in an amount of about 0.5 wt. % to about 20 wt. % of the total composition weight, about 0.5 wt. % to about 10 wt. % of the total composition weight, for example about 1.5 wt. %, about 3.75 wt. %, about 5 wt. %, or about 7.5 wt. % of the total composition weight in the case of a dentifrice, or for example about 0.5-2 wt. %, e.g., about 1% in the case of a mouthwash.

**[0017]** Abrasives: The compositions of the invention, e.g. Composition 1 et seq. include silica abrasives, and may comprise additional abrasives, e.g., a calcium phosphate abrasive, e.g., tricalcium phosphate ( $\text{Ca}_3(\text{PO}_4)_2$ ), hydroxyapatite ( $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$ ), or dicalcium phosphate dihydrate ( $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$ , also sometimes referred to herein as DiCal) or calcium pyrophosphate; calcium carbonate abrasive; or abrasives such as sodium metaphosphate, potassium metaphosphate, aluminum silicate, calcined alumina, bentonite or other siliceous materials, or combinations thereof.

**[0018]** Other silica abrasive polishing materials useful herein, as well as the other abrasives, generally have an average particle size ranging between about 0.1 and about 30 microns, about between 5 and about 15 microns. The silica abrasives can be from precipitated silica or silica gels, such as the silica xerogels described in U.S. Pat. No. 3,538,230, to Pader et al. and U.S. Pat. No. 3,862,307, to Digiulio. Particular silica xerogels are marketed under the trade name Syloid® by the W. R. Grace & Co., Davison Chemical Division. The precipitated silica materials include those marketed by the J. M. Huber Corp. under the trade name Zeodent®, including the silica carrying the designation Zeodent 115 and 119. These silica abrasives are described in U.S. Pat. No. 4,340,583, to Wason. In certain embodiments, abrasive materials useful in the practice of the oral care compositions in accordance with the invention include silica gels and precipitated amorphous silica having an oil absorption value of less than about 100 cc/100 g silica and in the range of about 45 cc/100 g to about 70 cc/100 g silica. Oil absorption values are measured using the ASTA Rub-Out Method D281. In certain embodiments, the silicas are colloidal particles having an average particle size of about 3 microns to about 12 microns, and about 5 to about 10 microns. Low oil absorption silica abrasives particularly useful in the practice of the 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

particles of colloidal silica having a water content of 29% by weight averaging about 7 to about 10 microns in diameter, and an oil absorption of less than about 70 cc/100 g of silica is an example of a low oil absorption silica abrasive useful in the practice of the present invention.

[0019] Foaming agents: The oral care compositions of the invention also may include an agent to increase the amount of foam that is produced when the oral cavity is brushed. Illustrative examples of agents that increase the amount of foam include, but are not limited to polyoxyethylene and certain polymers including, but not limited to, alginate polymers. The polyoxyethylene may increase the amount of foam and the thickness of the foam generated by the oral care carrier component of the present invention. Polyoxyethylene is also commonly known as polyethylene glycol ("PEG") or polyethylene oxide. The polyoxyethylenes suitable for this invention will have a molecular weight of about 200,000 to about 7,000,000. In one embodiment the molecular weight will be about 600,000 to about 2,000,000 and in another embodiment about 800,000 to about 1,000,000. Polyox® is the trade name for the high molecular weight polyoxyethylene produced by Union Carbide. The polyoxyethylene may be present in an amount of about 1% to about 90%, in one embodiment about 5% to about 50% and in another embodiment about 10% to about 20% by weight of the oral care carrier component of the oral care compositions of the present invention. Where present, the amount of foaming agent in the oral care composition (i.e., a single dose) is about 0.01 to about 0.9 % by weight, about 0.05 to about 0.5% by weight, and in another embodiment about 0.1 to about 0.2 % by weight.

[0020] Surfactants: The compositions useful in the invention may contain anionic surfactants, for example:

- i. water-soluble salts of higher fatty acid monoglyceride monosulfates, such as the sodium salt of the monosulfated monoglyceride of hydrogenated coconut oil fatty acids such as sodium N-methyl N-cocoyl taurate, sodium cocomonoglyceride sulfate,
- ii. higher alkyl sulfates, such as sodium lauryl sulfate,
- iii. higher alkyl-ether sulfates, e.g., of formula  $\text{CH}_3(\text{CH}_2)_m\text{CH}_2(\text{OCH}_2\text{CH}_2)_n\text{OSO}_3\text{X}$ , wherein m is 6-16, e.g., 10, n is 1-6, e.g., 2, 3 or 4, and X is Na or K, for example sodium laureth-2 sulfate ( $\text{CH}_3(\text{CH}_2)_{10}\text{CH}_2(\text{OCH}_2\text{CH}_2)_2\text{OSO}_3\text{Na}$ ).
- iv. higher alkyl aryl sulfonates such as sodium dodecyl benzene sulfonate (sodium lauryl benzene sulfonate)

- v. higher alkyl sulfoacetates, such as sodium lauryl sulfoacetate (dodecyl sodium sulfoacetate), higher fatty acid esters of 1,2 dihydroxy propane sulfonate, sulfocolaurate (N-2-ethyl laurate potassium sulfoacetamide) and sodium lauryl sarcosinate.

[0021] By “higher alkyl” is meant, e.g., C<sub>6-30</sub> alkyl. In particular embodiments, the anionic surfactant is selected from sodium lauryl sulfate and sodium ether lauryl sulfate. The anionic surfactant may be present in an amount which is effective, e.g., > 0.01% by weight of the formulation, but not at a concentration which would be irritating to the oral tissue, e.g., <10%, and optimal concentrations depend on the particular formulation and the particular surfactant. For example, concentrations used in a mouthwash are typically on the order of one tenth that used for a toothpaste. In one embodiment, the anionic surfactant is present in a toothpaste at from about 0.3% to about 4.5% by weight, e.g., about 1.5%. The compositions of the invention may optionally contain mixtures of surfactants, e.g., comprising anionic surfactants and other surfactants that may be anionic, cationic, zwitterionic or nonionic. Generally, surfactants are those which are reasonably stable throughout a wide pH range. Surfactants are described more fully, for example, in U.S. Pat. No. 3,959,458, to Agricola et al.; U.S. Pat. No. 3,937,807, to Haefele; and U.S. Pat. No. 4,051,234, to Gieske et al. In certain embodiments, the anionic surfactants useful herein include the water-soluble salts of alkyl sulfates having about 10 to about 18 carbon atoms in the alkyl radical and the water-soluble salts of sulfonated monoglycerides of fatty acids having about 10 to about 18 carbon atoms. Sodium lauryl sulfate, sodium lauroyl sarcosinate and sodium coconut monoglyceride sulfonates are examples of anionic surfactants of this type. In a particular embodiment, the composition of the invention, e.g., Composition 1, et seq., comprises sodium lauryl sulfate.

[0022] The surfactant or mixtures of compatible surfactants can be present in the compositions of the present invention in about 0.1% to about 5.0%, in another embodiment about 0.3% to about 3.0% and in another embodiment about 0.5% to about 2.0% by weight of the total composition.

[0023] Tartar control agents: In various embodiments of the present invention, the compositions comprise an anticalculus (tartar control) agent. Suitable anticalculus agents include without limitation phosphates and polyphosphates (for example pyrophosphates), polyaminopropanesulfonic acid (AMPS), hexametaphosphate salts, zinc citrate trihydrate, polypeptides, polyolefin sulfonates, polyolefin phosphates, diphosphonates. The invention thus

may comprise phosphate salts in addition to the zinc phosphate. In particular embodiments, these salts are alkali phosphate salts, i.e., salts of alkali metal hydroxides or alkaline earth hydroxides, for example, sodium, potassium or calcium salts. "Phosphate" as used herein encompasses orally acceptable mono- and polyphosphates, for example,  $P_{1-6}$  phosphates, for example monomeric phosphates such as monobasic, dibasic or tribasic phosphate; dimeric phosphates such as pyrophosphates; and multimeric phosphates, e.g., sodium hexametaphosphate. In particular examples, the selected phosphate is selected from alkali dibasic phosphate and alkali pyrophosphate salts, e.g., selected from sodium phosphate dibasic, potassium phosphate dibasic, dicalcium phosphate dihydrate, calcium pyrophosphate, tetrasodium pyrophosphate, tetrapotassium pyrophosphate, sodium tripolyphosphate, and mixtures of any of two or more of these. In a particular embodiment, for example the compositions comprise a mixture of tetrasodium pyrophosphate ( $Na_4P_2O_7$ ), calcium pyrophosphate ( $Ca_2P_2O_7$ ), and sodium phosphate dibasic ( $Na_2HPO_4$ ), e.g., in amounts of ca. 3-4% of the sodium phosphate dibasic and ca. 0.2-1% of each of the pyrophosphates. In another embodiment, the compositions comprise a mixture of tetrasodium pyrophosphate (TSPP) and sodium tripolyphosphate (STPP) ( $Na_5P_3O_{10}$ ), e.g., in proportions of TSPP at about 1-2% and STPP at about 7% to about 10%. Such phosphates are provided in an amount effective to reduce erosion of the enamel, to aid in cleaning the teeth, and/or to reduce tartar buildup on the teeth, for example in an amount of 2-20%, e.g., ca. 5-15%, by weight of the composition.

**[0024] *Flavoring Agents*:** The oral care compositions of the invention may also include a flavoring agent. Flavoring agents which are used in the practice of the present invention include, but are not limited to, 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. Certain embodiments employ the oils of peppermint and spearmint. The flavoring agent may be incorporated in the oral composition at a concentration of about 0.1 to about 5% by weight e.g. about 0.5 to about 1.5% by weight.

**[0025] *Polymers*:** The oral care compositions of the invention may also include additional polymers to adjust the viscosity of the formulation or enhance the solubility of other ingredients. Such additional polymers include polyethylene glycols, polysaccharides (e.g., cellulose

derivatives, for example carboxymethyl cellulose, or polysaccharide gums, for example xanthan gum or carrageenan gum). Acidic polymers, for example polyacrylate gels, may be provided in the form of their free acids or partially or fully neutralized water soluble alkali metal (e.g., potassium and sodium) or ammonium salts.

[0026] Silica thickeners, which form polymeric structures or gels in aqueous media, may be present. Note that these silica thickeners are physically and functionally distinct from the particulate silica abrasives also present in the compositions, as the silica thickeners are very finely divided and provide little or no abrasive action. Other thickening agents are carboxyvinyl polymers, carrageenan, hydroxyethyl cellulose and water soluble salts of cellulose ethers such as sodium carboxymethyl cellulose and sodium carboxymethyl hydroxyethyl cellulose. Natural gums such as karaya, gum arabic, and gum tragacanth can also be incorporated. Colloidal magnesium aluminum silicate can also be used as component of the thickening composition to further improve the composition's texture. In certain embodiments, thickening agents in an amount of about 0.5% to about 5.0% by weight of the total composition are used.

[0027] The compositions of the invention may include an anionic polymer, for example in an amount of from about 0.05 to about 5%. Such agents are known generally for use in dentifrice, although not for this particular application, useful in the present invention are disclosed in U.S. Pat. Nos. 5,188,821 and 5,192,531; and include synthetic anionic polymeric polycarboxylates, such as 1:4 to 4:1 copolymers of maleic anhydride or acid with another polymerizable ethylenically unsaturated monomer, preferably methyl vinyl ether/maleic anhydride having a molecular weight (M.W.) of about 30,000 to about 1,000,000, most preferably about 300,000 to about 800,000. These copolymers are available for example as Gantrez. e.g., AN 139 (M.W. 500,000), AN 119 (M.W. 250,000) and preferably S-97 Pharmaceutical Grade (M.W. 700,000) available from ISP Technologies, Inc., Bound Brook, N.J. 08805. The enhancing agents when present are present in amounts ranging from about 0.05 to about 3% by weight. Other operative polymers include those such as the 1:1 copolymers of maleic anhydride with ethyl acrylate, hydroxyethyl methacrylate, N-vinyl-2-pyrrolidone, or ethylene, the latter being available for example as Monsanto EMA No. 1103, M.W. 10,000 and EMA Grade 61, and 1:1 copolymers of acrylic acid with methyl or hydroxyethyl methacrylate, methyl or ethyl acrylate, isobutyl vinyl ether or N-vinyl-2-pyrrolidone. Suitable generally, are polymerized olefinically or ethylenically unsaturated carboxylic acids containing an activated carbon-to-carbon olefinic double bond and

at least one carboxyl group, that is, an acid containing an olefinic double bond which readily functions in polymerization because of its presence in the monomer molecule either in the alpha-beta position with respect to a carboxyl group or as part of a terminal methylene grouping. Illustrative of such acids are acrylic, methacrylic, ethacrylic, alpha-chloroacrylic, crotonic, beta-acryloxy propionic, sorbic, alpha-chlorosorbic, cinnamic, beta-styrylacrylic, muconic, itaconic, citraconic, mesaconic, glutaconic, aconitic, alpha-phenylacrylic, 2-benzyl acrylic, 2-cyclohexylacrylic, angelic, umbellic, fumaric, maleic acids and anhydrides. Other different olefinic monomers copolymerizable with such carboxylic monomers include vinylacetate, vinyl chloride, dimethyl maleate and the like. Copolymers contain sufficient carboxylic salt groups for water-solubility. A further class of polymeric agents includes a composition containing homopolymers of substituted acrylamides and/or homopolymers of unsaturated sulfonic acids and salts thereof, in particular where polymers are based on unsaturated sulfonic acids selected from acrylamidoalkane sulfonic acids such as 2-acrylamide 2 methylpropane sulfonic acid having a molecular weight of about 1,000 to about 2,000,000, described in U.S. Pat. No. 4,842,847, Jun. 27, 1989 to Zahid. Another useful class of polymeric agents includes polyamino acids containing proportions of anionic surface-active amino acids such as aspartic acid, glutamic acid and phosphoserine, e.g. as disclosed in U.S. Pat. No. 4,866,161 Sikes et al.

**[0028] Water:** The oral compositions may comprise significant levels of water. Water employed in the preparation of commercial oral compositions should be deionized and free of organic impurities. The amount of water in the compositions includes the free water which is added plus that amount which is introduced with other materials.

**[0029] Humectants:** Within certain embodiments of the oral compositions, it is also desirable to incorporate a humectant to prevent the composition from hardening upon exposure to air. Certain humectants can also impart desirable sweetness or flavor to dentifrice compositions. Suitable humectants include edible polyhydric alcohols such as glycerine, sorbitol, xylitol, propylene glycol as well as other polyols and mixtures of these humectants. In one embodiment of the invention, the principal humectant is glycerin, which may be present at levels of greater than 25%, e.g. 25-35% about 30%, with 5% or less of other humectants.

**[0030] Other optional ingredients:** In addition to the above-described components, the embodiments of this invention can contain a variety of optional dentifrice ingredients some of which are described below. Optional ingredients include, for example, but are not limited to,



adhesives, sudsing agents, flavoring agents, sweetening agents, additional antiplaque agents, abrasives, and coloring agents. These and other optional components are further described in U.S. Pat. No. 5,004,597, to Majeti; U.S. Pat. No. 3,959,458 to Agricola et al. and U.S. Pat. No. 3,937,807, to Haefele, all being incorporated herein by reference.

**[0031]** As used throughout, ranges are used as shorthand for describing each and every value that is within the range. Any value within the range can be selected as the terminus of the range. In addition, all references cited herein are hereby incorporated by referenced in their entireties. In the event of a conflict in a definition in the present disclosure and that of a cited reference, the present disclosure controls.

**[0032]** Unless otherwise specified, all percentages and amounts expressed herein and elsewhere in the specification should be understood to refer to percentages by weight. The amounts given are based on the active weight of the material.

### EXAMPLES

#### *Example 1*

**[0033]** Test dentifrices comprising 1% and 2% zinc citrate in combination with 5% arginine, 1450 ppm fluoride, and phosphates are prepared, together with control dentifrices comprising no zinc or no arginine, and the stability of the formulations, in particular the availability of zinc and fluoride, is measured after accelerated aging, as follows:

Table 1

Ingredient	A.1% Zinc	B. 2% Zinc	C. No Zinc	D. No Arginine
PEG600	3.00	3.00	3.00	3.00
CMC-7	0.65	0.65	0.65	0.75
Xanthan	0.20	0.20	0.20	0.20
Sorbitol	28.4	27.4	29.4	28.4
Glycerin	20.0	20.0	20.0	20.0
Saccharin	0.30	0.30	0.30	0.30
TSPP	0.50	0.50	0.50	0.50
cop Phosphate	0.25	0.25	0.25	0.25
dibasic Phosphate	3.50	3.50	3.50	3.50
Na Fluoride	0.32	0.32	0.32	0.32
Water	QS	QS	QS	QS
TiO <sub>2</sub>	0.50	0.50	0.50	0.50
Abrasive silica	8.00	8.00	8.00	8.00

Thickener silica	8.00	8.00	8.00	8.00
L-Arginine	5.00	5.00	5.00	-----
SLS	1.50	1.50	1.50	1.50
Brighter Flavor K91-5661	1.20	1.20	1.20	1.20
Zinc Citrate	1.00	2.00	-----	1.00
Initial @ room temperature				
% Arginine (4.5 - 5.5)	4.90	4.90	4.90	-----
FI (1250 - 1500 ppm)	1490	1490	1460	1390
% Zinc (0.5 - 0.35)	0.09	0.14	-----	0.08
pH (6.5 - 8.0)				
Cosmetic	Good	Good	Good	
1 Month @ 49°C				
% Arginine (4.5 - 5.5)	4.80	4.80	4.70	-----
FI (1250 - 1500 ppm)	1480	1500	1480	1330
% Zinc (0.5 - 0.35)	0.06	0.09	-----	
pH (6.5 - 8.0)				
Cosmetic	Good	Good	Good	
1 Month @ 40°C				
% Arginine (4.5 - 5.5)	4.90	4.80	4.70	-----
FI (1250 - 1500 ppm)	1420	1410	1480	1320
% Zinc (0.5 - 0.35)	0.10	0.10	-----	
pH (6.5 - 8.0)				
Cosmetic	Good	Good	Good	
1 Month @ -4°C				
% Arginine (4.5 - 5.5)	5.00	5.00	4.90	-----
FI (1250 - 1500 ppm)	1430	1470	1500	1370
% Zinc (0.5 - 0.35)	0.07	0.13	-----	
pH (6.5 - 8.0)				
Cosmetic	Good	Good	Good	
2 Months @ 49°C				
% Arginine (4.5 - 5.5)	4.70	4.70	4.60	
FI (1250 - 1500 ppm)	1480	1410	1460	1380
% Zinc (0.5 - 0.35)	0.06	0.10	-----	
pH (6.5 - 8.0)				
Cosmetic	Good	Good	Good	
2 Months @ 40°C				
% Arginine (4.5 - 5.5)	4.90	4.80	4.70	
FI (1250 - 1500 ppm)	1420	1470	1510	1290
% Zinc (0.5 - 0.35)	0.10	0.11	-----	
pH (6.5 - 8.0)				
Cosmetic	Good	Good	Good	

2 Months @ -4°C				
% Arginine (4.5 - 5.5)	5.00	4.90	5.00	
FI (1250 - 1500 ppm)	1440	1440	1450	1280
% Zinc (0.5 - 0.35)	0.08	0.13	- - - - -	
pH (6.5 - 8.0)				
Cosmetic	Good	Good	Good	
3 Months @ 49°C				
% Arginine (4.5 - 5.5)	4.70	4.80	4.50	
FI (1250 - 1500 ppm)	1470	1470	1480	
% Zinc (0.5 - 0.35)	0.06	0.08	- - - - -	
pH (6.5 - 8.0)				
Cosmetic	Good	Good	Good	
3 Months @ 40°C				
% Arginine (4.5 - 5.5)	4.80	4.80	4.70	
FI (1250 - 1500 ppm)	1470	1480	1430	
% Zinc (0.5 - 0.35)	0.09	0.13	- - - - -	
pH (6.5 - 8.0)				
Cosmetic	Good	Good	Good	
3 Months @ -4°C				
% Arginine (4.5 - 5.5)	5.00	4.90	4.90	
FI (1250 - 1500 ppm)	1430	1430	1430	
% Zinc (0.5 - 0.35)	0.12	0.18	- - - - -	
pH (6.5 - 8.0)				
Cosmetic	Good	Good	Good	

[0034] As will be noted, Formulation D, a zinc formulation without arginine, has significantly less available fluoride than the formulations with arginine, likely due to interaction of zinc and fluoride ions, but the formulations with 1% and 2% zinc citrate plus arginine have available fluoride levels approximately the same as the formulation without the zinc citrate, even after aging at low or high temperatures, suggesting that the presence of arginine enhances the availability of the fluoride in combination with zinc.

#### **Example 2**

[0035] The ability of the test and control formulations to deliver fluoride and zinc to the enamel is measured using electron spectroscopy for chemical analysis (ESCA, also known as x-ray photoelectron spectroscopy or XPS). ESCA is a surface analysis technique used for obtaining chemical information about the surfaces of solid materials. The materials characterization method utilizes an x-ray beam to excite a solid sample resulting in the emission of

photoelectrons. An energy analysis of these photoelectrons provides both elemental and chemical bonding information about a sample surface. The relatively low kinetic energy of the photoelectrons gives ESCA a sampling depth of approximately 30 Å. ESCA is used to analyze the mineral content of the enamel before and after use of test vs control dentifrices on polished and etched enamel substrates prepared and treated as described in the foregoing examples, confirming that zinc is delivered to the enamel surface and that zinc remains on the surface even after acid challenges, as well as confirming effective delivery of fluoride.

[0036] The ESCA data for the enamel samples treated with the various Zn / arginine / phosphate anti-erosion pastes of Example 1 are shown in Table 2 below, setting forth the elements detected and their respective atomic concentrations. All samples are analyzed after each polishing, etching and treatment step. For simplicity, only the mean composition for all samples is presented for the polished and etched surfaces. In all cases, three to four separate areas are analyzed for each sample. For the treated samples, the compositions of the individual areas, as well as the mean composition for each sample are presented.

[0037] C and N are detected on the polished and etched samples from surface organics. Ca and P are detected from the hydroxylapatite (HAP) in the enamel, with P/Ca ratios typical for enamel surfaces. The mean P/Ca ratio for the etched surfaces is slightly lower than that for the polished surfaces, indicating a reduction in surface phosphate relative to Ca occurs after etching. A low level of Zn is detected for the polished surfaces, which is removed by the etching. Fluoride is also detected for both the polished and etched surfaces at low levels. A low level of Na is also observed. Overall, the compositions of the polished and etched enamel surfaces are typical for bovine enamel.

[0038] C and N are detected on the surfaces of all the treated samples from surface organics. The C levels for all but the sample treated with the “no zinc” are higher than that for the etched surfaces, due to the presence of residual organics, most likely from the pastes. The N levels are also higher for the treated samples relative to the etched surfaces. For samples treated with pastes containing arginine, it is possible that some of the N is due to arginine on the surfaces. Thus, SIMS analysis is conducted on all the treated blocks to determine arginine deposition. The arginine molecular ion peak at 175 amu is detected only for the sample treated with the no Zn paste. This sample also exhibited the highest ESCA N level of all the treated samples. Thus for this sample, the higher N concentration determined by ESCA is at least in part due to the

presence of arginine on the surface. The arginine molecular ion peak is not observed for the other samples treated with arginine containing pastes. Arginine may still be present on these samples, but at levels below the SIMS detection limit. The ESCA N concentration for the sample treated with the arginine - free paste is similar to those for the remaining samples treated with arginine pastes. Thus the increase in N on these enamel surfaces can also be due to other non-arginine sources.

**[0039]** Ca and P are also detected on the surfaces of the samples, from the HAP in the enamel. The P/Ca ratios for the treated samples are higher than that for the etched surfaces, indicating an excess of phosphate relative to Ca. For all the samples, the Na concentrations are also significantly greater than that for the etched enamel. The higher phosphate and Na levels on the treated samples suggests that Na phosphate from the paste has been deposited on the enamel surfaces. Si is also detected in low amounts on the treated enamel, due to residual silica from the pastes.

**[0040]** For the enamel samples treated with the pastes containing zinc, elevated zinc levels are observed on the surface. As for the previous studies, the Zn/Ca ratios provide the best means for comparison of zinc uptake on the enamel surfaces. The Zn/Ca ratios for the enamel treated with the zinc citrate containing pastes are all the same. Thus the data suggest that neither arginine nor doubling the zinc citrate concentration have any discernible effect on zinc uptake.

**[0041]** The ESCA zinc peak positions can provide information on the chemical state of zinc on the enamel surfaces. The zinc peak positions for all the samples treated with zinc containing pastes are the same. This suggests that the zinc present on all the samples is in a similar chemical form. In addition, the zinc peak positions for the zinc paste treated samples are the same as those for the background zinc on the polished enamel surfaces. The background zinc inherently present in enamel is probably in the form of a zinc HAP. Thus the data suggest that the Zinc on the treated enamel may also be in the form of a zinc HAP.

**[0042]** F in the form of fluoride is detected on the surfaces of all the paste treated enamel samples. Relative fluoride uptake between samples is also best determined using the F/Ca ratios. The data indicate that enamel treated with the no zinc, 1% and 2% zinc citrate pastes had similar F/Ca ratios, suggesting similar F uptake. The enamel treated with the zinc citrate w/o arginine exhibited slightly lower F/Ca ratios, although we note that some variation

[0043] The ESCA results indicate that zinc deposition occurs for enamel treated with pastes containing either zinc citrate or zinc phosphate. Zinc deposition is greater for the paste containing zinc phosphate compared to the zinc citrate pastes. The data also suggest that zinc may be present on the surface in the form of a zinc-HAP. Elevated levels of fluoride are also observed for all the paste treated samples.

[0044] The detailed results of the analysis are presented in Table 2 (below).

Table 2

ESCA Analysis of Enamel - Zn / Arginine / PO <sub>4</sub> / NaF Anti-Erosion Paste														
Sample			Atomic Percent									Ratio		
			C	O	N	Ca	P	Zn	Na	F	Si	P/Ca	Zn/Ca	F/Ca
Polished - all 5 samples														
		mean	23.84	49.56	0.58	14.39	11.04	0.09	0.42	0.10	-	0.77	0.007	0.007
Etched - all 5 samples														
		mean	31.88	44.05	0.46	13.22	9.75	0.00	0.51	0.13	-	0.74	0.000	0.010
1% Zn citrate w/o arginine														
treated			40.57	36.10	0.82	8.78	8.32	0.54	3.35	0.48	1.05	0.95	0.062	0.055
			43.35	34.21	0.99	8.49	7.94	0.55	3.08	0.50	0.88	0.94	0.065	0.059
			44.50	33.64	1.00	8.47	7.82	0.53	2.88	0.49	0.67	0.92	0.063	0.058
		mean	42.81	34.65	0.94	8.58	8.03	0.54	3.10	0.49	0.87	0.94	0.063	0.057
1% Zn citrate w/ arginine														
treated			43.06	37.74	0.93	6.23	6.11	0.33	2.88	0.45	2.27	0.98	0.053	0.072
			42.48	36.77	0.74	7.25	6.84	0.45	2.50	0.51	2.43	0.94	0.062	0.070
		*	38.71	37.10	0.82	8.14	8.00	0.47	3.99	0.51	1.15	0.98	0.058	0.063
		mean	41.42	37.20	0.83	7.21	6.98	0.42	3.12	0.49	1.95	0.97	0.058	0.068
2% Zn citrate w/ arginine														
treated		*	47.28	31.68	1.19	7.15	7.42	0.39	2.42	0.49	1.15	1.04	0.055	0.069
			42.77	34.84	1.21	8.22	8.43	0.55	2.60	0.55	0.83	1.03	0.067	0.067
			43.07	34.28	1.26	7.94	8.22	0.51	3.12	0.52	1.08	1.04	0.064	0.065
		mean	44.37	33.60	1.22	7.77	8.02	0.48	2.71	0.52	1.02	1.03	0.062	0.067

[0045] As this data shows, the formulations comprising zinc and arginine deliver fluoride at nearly 20% higher levels than the formulation comprising zinc without arginine (F/Ca  $0.057 \pm 0.0016$  vs.  $0.068 \pm 0.0038$  for 1% zinc citrate and  $0.067 \pm 0.0016$  for 2% zinc citrate), which is

consistent with the data in the previous example that these formulations provide higher levels of available fluoride.

### **Example 3**

[0046] Dentifrice A of Example 1 containing 1% zinc citrate, together with arginine and fluoride, shows superior efficacy towards acid challenge compared to controls.

[0047] An *in vitro* methodology is used to determine the enamel protection activity of the formulation prototypes of Example 1. Enamel substrates (N = 6/8 per cell) are prepared by embedding bovine incisors in methacrylate-based resin and polishing with 600 and 1200 grit carbide paper consecutively. Care is taken not to penetrate the dentin layer while polishing the enamel to a mirror finish. Prior to testing, all enamel substrates are pre-etched with 5% citric acid for 30 sec. Half of a side of each substrate is masked with acid resistant tape to protect the surface as control surface. The model used to evaluate the products alternated 1-min product treatment periods with 2-min acid exposure periods according to the daily sequence of T – C – C – C – C – T (T = product treatment, C = acid challenge). The acid challenge is performed with a 1% aqueous solution of citric acid (unbuffered) adjusted to pH = 3.8 with NaOH. All enamel substrates are kept in a sterile artificial saliva solution at 37 °C while not undergoing treatment or challenge. This regimen is conducted for a total of five days, at the end of which a microhardness analysis is used to quantify the amount of enamel lost due to erosion on each enamel substrate on protected and exposed surfaces. The change in percentage hardness is calculated. Without treatment, using deionized water in place of test dentifrice, the change in percentage hardness is very high, approaching 80%, and only slightly reduced with treatment with a dentifrice without zinc (Formulation C), but is much reduced with treatment with Formulation A of Example 1.

Table 3

	DI Water	Formulation C	Formulation A
Average % reduction in hardness	78.28	70.16	46.44
Standard deviation	9.15	15.74	9.26

CLAIMS

1. An oral care composition comprising:  
from about 0.05 to about 5% by weight, of a zinc ion source;  
a fluoride ion source in an amount effective to deliver from about 500 to about 5,000 ppm fluoride, and  
from about 0.1 to about 10%, by weight, of a basic amino acid.
2. The composition of claim 1 wherein the zinc ion source is selected from zinc citrate, zinc sulfate, zinc silicate, zinc lactate, zinc phosphate, zinc oxide, and combinations thereof, in an amount effective to inhibit erosion.
3. The composition according to any of the preceding claims wherein the basic amino acid is arginine.
4. The composition according to any of the preceding claims in the form of a dentifrice comprising an abrasive.
5. The composition according to any of the preceding claims wherein the amount of zinc is 0.5 to 4% by weight.
6. The composition of any of the foregoing claims comprising one or more abrasives, one or more humectants, and one or more surfactants.
7. The composition of any of the foregoing claims further comprising an effective amount of one or more alkali phosphate salts.
8. The composition of any of the foregoing claims further comprising an effective amount of one or more antibacterial agents.
9. The composition of any of the foregoing claims further comprising a whitening agent.



10. The composition of any of the foregoing claims further comprising one or more sources of zinc ion in addition to the zinc phosphate.
11. The composition of any of the foregoing claims wherein the pH of the composition is basic.
12. The composition of any of the foregoing claims comprising
  - 1 to 3% zinc citrate;
  - 1 to 8% arginine;
  - 2 to 8% alkali phosphate salts selected from sodium phosphate dibasic, potassium phosphate dibasic, dicalcium phosphate dihydrate, tetrasodium pyrophosphate, tetrapotassium pyrophosphate, calcium pyrophosphate, sodium tripolyphosphate, and a combination of two or more thereof;
  - 700 to 2000 ppm fluoride;
  - in a silica abrasive dentifrice base.
13. Use of a basic amino acid to enhance fluoride delivery in an oral care composition comprising a zinc ion source and a fluoride ion source.
14. A method of treating or reducing dental enamel erosion comprising administering a composition according to any of claims 1 to 12 to the oral cavity of a subject in need thereof.
15. The composition according to any of claims 1 to 12 for use in treating or reducing dental enamel erosion.

## INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2012/067994

## A. CLASSIFICATION OF SUBJECT MATTER

INV. A61K8/27 A61K8/44 A61Q11/00 A61K8/21  
ADD.

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)

A61K A61Q

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 practicable, search terms used)

EPO-Internal, BIOSIS, CHEM ABS Data, EMBASE, EMBL, INSPEC, PAJ, WPI Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 1 203 575 A2 (UNILEVER) 8 May 2002 (2002-05-08)	1,2,4-6
Y	paragraph [0005] - paragraph [0006] examples paragraph [0015] - paragraph [0025] -----	7-11
X	WO 2011/123123 A1 (COLGATE PALMOLIVE) 6 October 2011 (2011-10-06) paragraph [0001] paragraph [0011] - paragraph [0015] paragraph [0019] - paragraph [0022] paragraph [0032] paragraph [0036] - paragraph [0037] claims ----- -/-	1-6, 13-15



Further documents are listed in the continuation of Box C.



See patent family annex.

## \* Special categories of cited documents :

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Date of the actual completion of the international search

30 August 2013

Date of mailing of the international search report

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Irwin, Lucy

## INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2012/067994

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WO 2011/162756 A1 (COLGATE PALMOLIVE)  29 December 2011 (2011-12-29)  paragraph [0008]  paragraph [0012]  paragraph [0024] - paragraph [0028]  paragraph [0037]  examples II, C  claims</p> <p style="text-align: center;">-----</p>	1-3,6-8
Y	<p>GB 2 481 630 A (TAYLOR ET AL)  4 January 2012 (2012-01-04)  page 1 - page 2  page 8, paragraph 1  page 11 - page 12  claims</p> <p style="text-align: center;">-----</p>	1-15
Y	<p>EP 0 074 082 A2 (RICHARDSON VICKS)  16 March 1983 (1983-03-16)  page 1 - page 5  page 9  examples</p> <p style="text-align: center;">-----</p>	1-15
A	<p>US 2009/202451 A1 (COLGATE PALMOLIVE)  13 August 2009 (2009-08-13)  paragraph [0004] - paragraph [0005]  paragraph [0010]  paragraph [0019] - paragraph [0021]  paragraph [0142] - paragraph [0144]  paragraph [0153] - paragraph [0157]</p> <p style="text-align: center;">-----</p>	1-15
A	<p>EP 0 428 492 A2 (MONSANTO)  22 May 1991 (1991-05-22)  page 1, line 4 - line 12  claims; examples</p> <p style="text-align: center;">-----</p>	1-15

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