ORAL CARE PRODUCT AND METHODS OF USE AND MANUFACTURE THEREOF

[0001] This application claims the benefit of U.S. Ser. No. 61/027,432 filed February 8, 2008, U.S. Ser. No. 61/027,431 filed February 8, 2008 and U.S. Ser. No. 61/027,420 filed February 8, 2008, the contents of which are incorporated herein by reference.

FIELD OF THE INVENTION

[0002] This invention relates to oral care compositions comprising a basic amino acid in free or salt form, an anionic surfactant, and optional additional agents, and to methods of using and of making these compositions.

BACKGROUND OF THE INVENTION

[0003] Arginine and other basic amino acids have been proposed for use in oral care and are believed to have benefits in combating cavity formation and tooth sensitivity. Combining these basic amino acids with minerals having oral care benefits, e.g., fluoride and calcium, to form an oral care product having acceptable long term stability, however, has proven challenging. In particular, the basic amino acid may raise the pH and facilitate dissociation of calcium ions that can react with fluoride ions to form an insoluble precipitate. Moreover, the higher pH has the potential to cause irritation. At neutral pH or acidic pH, however, a system utilizing arginine bicarbonate (which the art teaches is preferred) may release carbon dioxide, leading to bloating and bursting of the containers. Moreover, it might be expected that lowering the pH to neutral or acidic conditions would reduce the efficacy of the formulation because the arginine may form an insoluble arginine-calcium complex that has a poorer affinity for the tooth surface, and moreover that lowering the pH would reduce any effect the formulation might have on buffering cariogenic lactic acid in the mouth. Partly because of these unaddressed formulation hurdles and partly because arginine has generally been viewed in the art as a potential alternative to fluoride rather than a co-active, there has been little motivation to make oral care products comprising both arginine and fluoride. Additional hurdles are potentially posed by addition of an antimicrobial agent. Commercially available arginine-based toothpaste, such as ProClude® and DenClude®, for example, contain arginine bicarbonate and calcium carbonate, but not fluoride nor any antimicrobial agent.

[0004] At the same time, the value of antimicrobial agents, such as triclosan, in toothpaste has been recognized by many dentists. These agents however are challenging to deliver in effective amounts to the teeth and gums, and their solubility, delivery and retention on the teeth is formulation dependent. For example, triclosan (5-chloro-2-(2,4-

dichlorophenoxy)phenol) is only slightly soluble in water.

[0005] Accordingly, there is a need for a stable oral care product that provides a basic amino acid, beneficial minerals such as fluoride and calcium, improved activity against bacteria, and improved delivery of antimicrobial agents.

BRIEF SUMMARY OF THE INVENTION

[0006] It is now surprisingly discovered that a basic amino acid such as arginine in combination with an anionic surfactant can reduce bacterial attachment and biofilm formation and additionally dramatically enhance solubility, delivery, retention and antibacterial effectiveness of an antibacterial agent such as triclosan.

[0007] The invention thus encompasses oral care compositions and methods of using the same that are effective in inhibiting or reducing the accumulation of plaque, reducing levels of acid producing (cariogenic) bacteria, remineralizing teeth, and inhibiting or reducing gingivitis. The invention also encompasses compositions and methods to clean the oral cavity and provide improved methods of promoting oral health and/or systemic health, including cardiovascular health, e.g., by reducing potential for systemic infection via the oral tissues.

[0008] The invention thus comprises an oral care composition (a Composition of the Invention), e.g., a dentifrice, comprising

i. an effective amount of a basic amino acid, in free or salt form, e.g., arginine;

ii. an effective amount of an anionic surfactant, e.g., sodium lauryl sulfate; and

an additional agent selected from one or more of an antibacterial agent, e.g., a halogenated diphenyl ether, e.g., triclosan; an effective amount of a fluoride source, e.g., a soluble fluoride salt; and/or an anionic polymer, e.g., a copolymer of methyl vinyl ether and maleic anhydride (PVM/MA). The invention thus encompasses in one embodiment a toothpaste comprising an arginine salt, e.g., arginine hydrochloride, arginine phosphate or arginine bicarbonate; triclosan; an anionic surfactant, e.g., sodium lauryl sulfate; a soluble fluoride salt, e.g., sodium monofluorophosphate or sodium fluoride.

[0009] In one embodiment, the invention encompasses a Composition of the Invention (Composition 1.1) further comprising a particulate, the composition having a RDA of less than about 200, e.g., less than about 160, e.g., about 40 to about 140, e.g., comprising at least about 5%, e.g., at least 20% of a particulate having a d50 less than about 5 micrometers, e.g., silica having a d50 of about 3 to about 4 micrometers or precipitated calcium carbonate having a d50 of about 0.5 to about 3 micrometers.

[0010] In particular embodiments, the Compositions of the Invention are in the form of a dentifrice comprising additional ingredients selected from one or more of water, abrasives, surfactants, foaming agents, vitamins, polymers, enzymes, humectants, thickeners, antimicrobial agents, preservatives, flavorings, colorings and/or combinations thereof.

[0011] Without intending to be bound by a particular theory, it is hypothesized that a significant factor in the beneficial effect of arginine is that arginine and other basic amino acids can be metabolized by certain types of bacteria, e.g., *S. sanguis* which are not cariogenic and which compete with cariogenic bacteria such as *S. mutans*, for position on the teeth and in the oral cavity. The arginolytic bacteria can use arginine and other basic amino acids to produce ammonia, thereby raising the pH of their environment, while cariogenic bacteria metabolize sugar to produce lactic acid, which tends to lower the plaque pH and demineralize the teeth, ultimately leading to cavities. It is believed that regular use of a Composition of the Invention, over time, will lead to a relative increase in the arginolytic bacteria and a relative decrease in the cariogenic bacteria, resulting in a higher plaque pH, in effect immunizing the teeth against cariogenic bacteria and their detrimental effects. It is believed that this pH-raising effect may be mechanistically separate from and complementary to the effect of fluoride in promoting remineralization and strengthening the tooth enamel.

[0012] Irrespective of the precise mechanism, however, it is surprisingly found that the combination of fluoride and a basic amino acid, e.g., arginine, in an oral care product according to particular embodiments of the present invention produces unexpected benefits beyond and qualitatively different from what can be observed using compositions comprising effective amounts of either compound separately, in promoting remineralization, repairing pre-carious lesions, and enhancing oral health. It has moreover been found that this action can be further enhanced by addition of a small particle abrasive, which may act to help fill microtubules in the dentin.

[0013] The presence of a basic amino acid in combination with an anionic surfactant is also surprisingly found to reduce bacterial adhesion to the tooth surface.

[0014] Of particular relevance to this invention, the basic amino acid together with an anionic surfactant substantially enhances solubilization, release, delivery, deposition, and effectiveness of active agents, for example antimicrobial agents, such as triclosan.

[0015] The reduction in bacterial adhesion and the improved delivery and retention of an antibacterial agent, e.g., triclosan, is further enhanced by the presence of an anionic polymer,

e.g., a polycarboxylate, e.g., PVM/MA. The invention thus further encompasses methods to (i) reduce or inhibit formation of dental caries, (ii) reduce, repair or inhibit early enamel lesions, e.g., as detected by quantitative light-induced fluorescence (QLF) or electrical caries measurement (ECM), (iii) reduce or inhibit demineralization and promote remineralization of the teeth, (iv) reduce hypersensitivity of the teeth, (v) reduce or inhibit gingivitis, (vi) promote healing of sores or cuts in the mouth, (vii) reduce levels of acid producing bacteria, (viii) increase relative levels of arginolytic bacteria, (ix) inhibit microbial biofilm formation in the oral cavity, (x) raise and/or maintain plaque pH at levels of at least pH 5.5 following sugar challenge, (xi) reduce plaque accumulation, (xii) treat dry mouth; (xiii) enhance systemic health, including cardiovascular health, e.g., by reducing potential for systemic infection via the oral tissues, (xiv) reduce erosion of the teeth, and/or (xv) clean and/or whiten the teeth and clean the oral cavity, comprising applying a Composition of the Invention to the oral cavity, e.g., by applying a Composition of the Invention to the oral cavity of a patient in need thereof.

DETAILED DESCRIPTION OF THE INVENTION

[0016] The invention thus comprises an oral care composition (Composition 1.0) comprising

i. an effective amount of a basic amino acid, e.g., arginine, in free or salt form;

ii. an anionic surfactant, e.g., sodium lauryl sulfate; and

iii. an additional agent selected from one or more of an effective amount of an active agents, e.g., an antimicrobial agent, e.g., triclosan; an effective amount of a fluoride source, e.g., a soluble fluoride salt; and/or an anionic polymer, e.g., a copolymer of methyl vinyl ether and maleic anhydride;

for example any of the following compositions:

1.0.1. Composition 1.0 wherein the basic amino acid is arginine, lysine, citrullene, ornithine, creatine, histidine, diaminobutanoic acid, diaminoproprionic acid, salts thereof and/or combinations thereof.

1.0.2. Composition 1.0 or 1.0.1 wherein the basic amino acid has the L-configuration.

1.0.3. Any of the preceding compositions is provided in the form of a salt of a di- or tri-peptide comprising the basic amino acid.

1.0.4. Any of the preceding compositions wherein the basic amino acid is arginine.

1.0.5. Any of the preceding compositions wherein the basic amino acid is L-arginine.

1.0.6. Any of the preceding compositions wherein the basic amino acid is partially or wholly in salt form.

1.0.7. Composition 1.0.6 wherein the basic amino acid is arginine phosphate.

1.0.8. Composition 1.0.6 wherein the basic amino acid is in the form of arginine hydrochloride.

1.0.9. Composition 1.0.6 wherein the basic amino acid is arginine sulfate.

1.0.10. Composition 1.0.6 wherein the basic amino acid is arginine bicarbonate.

1.0.11. Any of the preceding compositions wherein a salt of the basic amino acid is formed in situ in the formulation by neutralization of the basic amino acid with an acid or a salt of an acid.

1.0.12. Any of the preceding compositions wherein the salt of the basic amino acid is formed by neutralization of the basic amino acid to form a premix prior to combination with the fluoride salt.

1.0.13. Any of the preceding compositions wherein the basic amino acid is present in an amount corresponding to about 0.1 to about 20%, e.g., about 1 wt % to about 10 wt % , for example about 3% to about 10% of the total composition weight. the weight of the basic amino acid being calculated as free base form.

1.0.14. Composition 1.0.11 wherein the basic amino acid is present in an amount of about 7.5 wt % of the total composition weight.

1.0.15. Composition 1.0.11 wherein the basic amino acid is present in an amount of about 5 wt % of the total composition weight.

1.0.16. Composition 1.0.11 wherein the basic amino acid is present in an amount of about 3.75 wt % of the total composition weight.

1.0.17. Composition 1.0.11 wherein the basic amino acid is present in an amount of about 1.5 wt % of the total composition weight.

1.0.18. Any of the preceding compositions wherein the fluoride salt is 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.

1.0.19. Any of the preceding compositions wherein the fluoride salt is a fluorophosphate.

1.0.20. Any of the preceding composition wherein the fluoride salt is sodium monofluorophosphate.

1.0.21. Any of the preceding compositions where the fluoride salt is sodium fluoride.

1.0.22. Any of the preceding compositions wherein the fluoride salt is present in an amount of about 0.01 wt. % to about 2 wt. % of the total composition weight.

1.0.23. Any of the preceding compositions wherein the fluoride salt provides fluoride ion in an amount of about 0.1 to about 0.2 wt. % of the total composition weight.

1.0.24. Any of the preceding compositions wherein the soluble fluoride salt provides fluoride ion in an amount of from about 50 to about 25,000 ppm.

1.0.25. Any of the preceding compositions which is a mouthwash having 100 to about 250 ppm available fluoride ion.

1.0.26. Any of the preceding compositions which is a dentifrice having about 750 to about 2000 ppm available fluoride ion.

1.0.27. Any of the preceding compositions wherein the composition comprises about 750 to about 2000 ppm fluoride ion.

1.0.28. Any of the preceding compositions wherein the composition comprises about 1000 to about 1500 ppm fluoride ion.

1.0.29. Any of the preceding compositions wherein the composition comprises about 1450 ppm fluoride ion.

1.0.30. Any of the preceding compositions wherein the pH is about 6 to about 9, e.g., about 6.5 to about 7.4 or about 7.5 to about 9.

1.0.31. Any of the preceding compositions wherein the pH is about 6.5 to about 7.4.

1.0.32. Any of the preceding compositions wherein the pH is about 6.8 to about 7.2.

1.0.33. Any of the preceding compositions wherein the pH is approximately neutral.

1.0.34. Any of the preceding compositions further comprising an abrasive or particulate.

1.0.35. The immediately preceding composition wherein the abrasive or particulate is selected from sodium bicarbonate, calcium phosphate (e.g., dicalcium phosphate dihydrate),

calcium sulfate, calcium carbonate (e.g., precipitated calcium carbonate), silica (e.g., hydrated silica), iron oxide, hydroxyapatite, aluminum oxide, perlite, plastic particles, e.g., polyethylene, and combinations thereof.

1.0.36. The immediately preceding composition wherein the abrasive or particulate is selected from a calcium phosphate (e.g., dicalcium phosphate dihydrate), calcium sulfate, precipitated calcium carbonate, silica (e.g., hydrated silica), and combinations thereof.

1.0.37. Any of the preceding compositions comprising an abrasive in an amount of about 15 wt % to about 70 wt % of the total composition weight.

1.0.38. Any of the preceding compositions comprising a small particle abrasive fraction of at least about 5% having a d50 of less than about 5 micrometers.

1.0.39. Any of the preceding compositions having a RDA of less than 150, e.g., about 40 to about 140.

1.0.40. Any of the preceding compositions further comprising an anti-calculus agent.

1.0.41. Any of the preceding compositions further comprising an anti-calculus agent which is a polyphosphate, e.g., pyrophosphate, tripolyphosphate, or hexametaphosphate, e.g., in sodium salt form.

1.0.42. Any of the preceding compositions wherein the anionic surfactant is selected from

a. water-soluble salts of higher fatty acid monoglyceride monosulfates (e.g., the sodium salt of the monosulfated monoglyceride of hydrogenated coconut oil fatty acids such as sodium N-methyl N-cocoyl taurate, sodium cocomo-glyceride sulfate),

b. higher alkyl sulfates, e.g., sodium lauryl sulfate,

c. higher alkyl-ether sulfates, e.g., of formula $CH_3(CH_2)_mCH_2(OCH_2CH_2)_nOSO_3X$, 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 ($CH_3(CH_2)_{10}CH_2(OCH_2CH_2)_2OSO_3Na$)),

d. higher alkyl aryl sulfonates (such as sodium dodecyl benzene sulfonate (sodium lauryl benzene sulfonate)),

e. 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),

f. and mixtures thereof.

By "higher alkyl" is meant, e.g., C_{6-30} alkyl. In particular embodiments, the anionic surfactant is selected from sodium lauryl sulfate and sodium ether lauryl sulfate.

1.0.43. Any of the preceding compositions wherein the anionic surfactant is selected from sodium lauryl sulfate, sodium ether lauryl sulfate, and mixtures thereof.

1.0.44. Any of the preceding compositions wherein the anionic surfactant is present in an amount of from about 0.3% to about 4.5% by weight.

1.0.45. Any of the preceding compositions additionally comprising surfactants selected from cationic, zwitterionic, and nonionic surfactants, and mixtures thereof.

1.0.46. Any of the preceding compositions further comprising at least one humectant.

1.0.47. Any of the preceding compositions further comprising at least one humectant selected from glycerin, sorbitol and combinations thereof.

1.0.48. Any of the preceding compositions further comprising xylitol.

1.0.49. Any of the preceding compositions further comprising at least one polymer.

1.0.50. Any of the preceding compositions further comprising at least one polymer selected from polyethylene glycols, polyvinylmethyl ether maleic acid copolymers, polysaccharides (e.g., cellulose derivatives, for example carboxymethyl cellulose, or polysaccharide gums, for example xanthan gum or carrageenan gum), and combinations thereof.

1.0.51. Any of the preceding compositions further comprising gum strips or fragments.

1.0.52. Any of the preceding compositions further comprising flavoring, fragrance and/or coloring.

1.0.53. Any of the preceding compositions further comprising water.

1.0.54. Any of the preceding compositions further 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.

1.0.55. Any of the preceding compositions further comprising an anti-inflammatory compound, e.g., an inhibitor of at least one of host pro-inflammatory factors selected from matrix metalloproteinases (MMP's), cyclooxygenases (COX), PGE_2, interleukin 1 (IL-1), IL-1β converting enzyme (ICE), transforming growth factor β1 (TGF-β1), inducible nitric oxide synthase (iNOS), hyaluronidase, cathepsins, nuclear factor kappa B (NF-κB), and IL-1 Receptor Associated Kinase (IRAK), e.g., selected from aspirin, ketorolac, flurbiprofen, ibuprofen, naproxen, indomethacin, aspirin, ketoprofen, piroxicam, meclofenamic acid, nordihydoguaiaretic acid, and mixtures thereof.

1.0.56. Any of the preceding compositions further comprising an antioxidant, e.g., selected from the group consisting of Co-enzyme Q10, PQQ, Vitamin C, Vitamin E, Vitamin A, anethole-dithiothione, and mixtures thereof.

1.0.57. Any of the preceding compositions wherein the anti-bacterial is poorly soluble, e.g., no more soluble than triclosan.

1.0.58. Any of the preceding compositions further comprising triclosan.

1.0.59. Any of the preceding compositions further comprising triclosan and xylitol.

1.0.60. Any of the preceding compositions further comprising triclosan, xylitol, and precipitated calcium carbonate.

1.0.61. Any of the preceding compositions further comprising triclosan and a Zn^{2+} ion source (e.g., zinc citrate).

1.0.62. Any of the preceding compositions further comprising an antibacterial agent in an amount of about 0.01 to about 5 wt. % of the total composition weight.

1.0.63. Any of the preceding compositions further comprising triclosan in an amount of about 0.01 to about 1 wt. % of the total composition weight.

1.0.64. Any of the preceding compositions further comprising triclosan in an amount of

about 0.3% of the total composition weight.

1.0.65. Any of the preceding compositions further comprising triclosan and a Zn^{2+} ion source e.g., zinc citrate.

1.0.66. Any of the preceding compositions further comprising a whitening agent.

1.0.67. Any of the preceding compositions further comprising a whitening agent selected from a whitening active selected from the group consisting of peroxides, metal chlorites, perborates, percarbonates, peroxyacids, hypochlorites, and combinations thereof.

1.0.68. 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), or hydrogen peroxide polymer complexes such as hydrogen peroxide-polyvinyl pyrrolidone polymer complexes.

1.0.69. Any of the preceding compositions further comprising an agent that interferes with or prevents bacterial attachment, e.g., solbrol or chitosan.

1.0.70. 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.

1.0.71. 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.

1.0.72. Any of the preceding compositions further comprising a physiologically acceptable potassium salt, e.g., potassium nitrate or potassium chloride, in an amount effective to reduce dentinal sensitivity.

1.0.73. Any of the preceding compositions further comprising from about 0.1% to about 7.5% of a physiologically acceptable potassium salt, e.g., potassium nitrate and/or potassium chloride.

1.0.74. Any of the preceding compositions which is a toothpaste comprising an arginine salt, e.g., arginine hydrochloride, arginine phosphate or arginine bicarbonate; triclosan; an anionic surfactant, e.g., sodium lauryl sulfate; and a soluble fluoride salt, e.g., sodium

monofluorophosphate or sodium fluoride.

1.0.75. Any of the preceding compositions effective upon application to the oral cavity, e.g., with brushing, to (i) reduce or inhibit formation of dental caries, (ii) 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), (iii) reduce or inhibit demineralization and promote remineralization of the teeth, (iv) reduce hypersensitivity of the teeth, (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 arginolytic bacteria, (ix) inhibit microbial biofilm formation in the oral cavity, (x) raise and/or maintain plaque pH at levels of at least pH 5.5 following sugar challenge, (xi) reduce plaque accumulation, (xii) treat, relieve or reduce dry mouth, (xiii) clean the teeth and oral cavity (xiv) reduce erosion, (xv) whiten teeth, (xvi) immunize the teeth against cariogenic bacteria; and/or (xvii) promote systemic health, including cardiovascular health, e.g., by reducing potential for systemic infection via the oral tissues.

1.0.76. A composition obtained or obtainable by combining the ingredients as set forth in any of the preceding compositions.

1.0.77. Any of the preceding compositions in a form selected from mouth rinse, toothpaste, tooth gel, tooth powder, non-abrasive gel, mousse, foam, mouth spray, lozenge, oral tablet, dental implement, and pet care product.

1.0.78. Any of the preceding compositions wherein the composition is toothpaste.

1.0.79. Any of the preceding compositions wherein the composition is a toothpaste optionally further comprising one or more of one or more of water, abrasives, surfactants, foaming agents, vitamins, polymers, enzymes, humectants, thickeners, antimicrobial agents, preservatives, flavorings, colorings and/or combinations thereof.

1.0.80. Any of the preceding compositions 1.0 – 1.0.78 wherein the composition is a mouthwash.

1.0.81. Any of the preceding compositions further comprising a breath freshener, fragrance or flavoring.

[0017] In another embodiment, the invention encompasses a Composition of the Invention (Composition 1.1) e.g., according to any of the preceding Compositions 1.0 – 1.0.81, comprising

i. an effective amount of a salt of a basic amino acid;

ii. an effective amount of a soluble fluoride salt;

iii. an anionic surfactant, e.g., sodium lauryl sulfate;

iv. an anionic polymer, e.g., a copolymer of methyl vinyl ether and maleic anhydride; and

v. an antibacterial agent, e.g., triclosan.

[0018] In another embodiment, the invention encompasses a Composition of the Invention (Composition 1.2) e.g., according to any of the preceding Compositions 1.0 – 1.0.81, comprising

i. an effective amount of a salt of a basic amino acid;

ii. an antibacterial agent, e.g., triclosan;

iii. an effective amount of a soluble fluoride salt; and

iv. small particle abrasive, such that the composition has a RDA of less than about 160, e.g., about 40 to about 140, e.g., comprising at least about 5%, e.g., at least about 20% of an abrasive having a d50 less than about 5 micrometers, e.g., silica having a d50 of about 3 to about 4 micrometers.

[0019] In another embodiment, the invention encompasses a method (Method 2) to improve oral health comprising applying an effective amount of the oral composition of any of the embodiments under Compositions 1.0, 1.1, or 1.2, to the oral cavity of a subject in need thereof, e.g., a method to

i. reduce or inhibit formation of dental caries,

ii. reduce, repair or inhibit early enamel lesions, e.g., as detected by quantitative light-induced fluorescence (QLF) or electrical caries measurement (ECM),

iii. reduce or inhibit demineralization and promote remineralization of the teeth,

iv. reduce hypersensitivity of the teeth,

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 arginolytic bacteria,

ix. inhibit microbial biofilm formation in the oral cavity,

x. raise and/or maintain plaque pH at levels of at least about pH 5.5 following sugar challenge,

xi. reduce plaque accumulation,

xii. treat dry mouth,

xiii. enhance systemic health, including cardiovascular health, e.g., by reducing potential for systemic infection via the oral tissues,

xiv. whiten teeth,

xv. to reduce erosion of the teeth,

xvi. immunize the teeth against cariogenic bacteria, and/or

xvii. clean the teeth and oral cavity.

[0020] The invention further comprises the use of arginine in the manufacture of a Composition of the Invention, e.g., for use in any of the indications set forth in Method 2.

[0021] The invention further provides an oral care composition comprising a basic amino acid, in free or salt form, and an anionic surfactant for reducing the adhesion of bacteria to tooth surfaces in an oral cavity of a subject.

[0022] The invention further provides the use of a basic amino acid, in free or salt form, in an oral care composition comprising an anionic surfactant for reducing the adhesion of bacteria to tooth surfaces in an oral cavity of a subject.

[0023] The invention further provides the use of a basic amino acid, in free or salt form, for the manufacture of a medicament which includes an anionic surfactant, for use in reducing the adhesion of bacteria to tooth surfaces in an oral cavity of a subject.

[0024] The invention further provides a method of reducing the adhesion of bacteria to tooth surfaces in an oral cavity of a subject, the method comprising treating the oral cavity with an oral care composition comprising a basic amino acid, in free or salt form, and an anionic surfactant.

[0025] It may therefore be seen by the skilled practitioner in the oral care art that a surprising technical effect and advantage of reduced bacterial adhesion to the teeth can result from the formulation, and use, of an oral care composition, for example a dentifrice, in accordance with one or more aspects of the invention, which are directed to the provision

of combinations of active components or ingredients, and preferably their respective amounts, within the composition.

[0026] Levels of active ingredients will vary based on the nature of the delivery system and the particular active. For example, the basic amino acid may be present at levels from, e.g., about 0.1 to about 20 wt %(expressed as weight of free base), e.g., about 0.1 to about 3 wt % for a mouth rinse, 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 may be present at levels of, e.g., about 25 to about 25,000 ppm, for example about 25 to about 250 ppm for a mouth rinse, 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 will vary similarly, with levels used in toothpaste being e.g., about 5 to about 15 times greater than used in mouth rinse. For example, a triclosan mouth rinse may contain, e.g., about 0.03 wt % triclosan while a triclosan toothpaste may contain, e.g., about 0.3 wt % triclosan.

Basic Amino Acids

[0027] The basic amino acids which can be used in the compositions and methods of the invention include not only naturally occurring basic amino acids, such as arginine, lysine, and histidine, but also any basic amino acids having a carboxyl group and an amino group in the molecule, which are water-soluble and provide an aqueous solution with a pH of about 7 or greater.

[0028] Accordingly, basic amino acids include, but are not limited to, arginine, lysine, citrullene, ornithine, creatine, histidine, diaminobutanoic acid, diaminoproprionic acid, salts thereof or combinations thereof. In a particular embodiment, the basic amino acids are selected from arginine, citrullene, and ornithine.

[0029] In certain embodiments, the basic amino acid is arginine, for example, l-arginine, or a salt thereof.

[0030] In some embodiments the basic amino acid comprises at least one intermediate produced in the arginine deiminase system. The intermediates produced in the arginine deiminase system may be useful in an oral care composition to provide plaque neutralization for caries control and/or prevention. Arginine is a natural basic amino acid that may be found in the oral cavity. Arginine in the mouth may be utilized by certain dental plaque bacterial strains such as *S. sanguis*, *S. gordonii*, *S. parasanguis*, *S. rattus*, *S. milleri*, *S. anginosus*, *S.*

faecalis, *A. naeslundii*, *A. odonolyticus*, *L. cellobiosus*, *L. brevis*, *L. fermentum*, *P. gingivalis*, and *T. denticola* for their survival. Such organisms may perish in an acidic environment that may be present at areas close to the tooth surface where acidogenic and aciduric cariogenic strains may use sugars to produce organic acids. Thus, these arginolytic strains may break down arginine to ammonia to provide alkalinity to survive and, in addition, buffer the plaque and make a hostile environment for the cariogenic systems.

[0031] Such arginolytic organisms may catabolize arginine by an internal cellular enzyme pathway system called the "arginine deiminase system" whereby intermediates in the pathway are formed. In this pathway, L-arginine may be broken down to L-citrulline and ammonia by arginine deiminase. L-citrulline may then be broken down by ornithane trancarbamylase in the presence of inorganic phosphate to L-ornithine and carbamyl phosphate. Carbamate kinase may then break down carbamyl phosphate to form another molecule of ammonia and carbon dioxide, and in the process also forms ATP (adenosine 5'-triphosphate). ATP may be used by the arginolytic bacteria as an energy source for growth. Accordingly, when utilized, the arginine deiminase system may yield two molecules of ammonia.

[0032] It has been found that, in some embodiments, the ammonia may help in neutralizing oral plaque pH to control and/or prevent dental caries.

[0033] The oral care composition of some embodiments of the present invention may include intermediates produced in the arginine deiminase system. Such intermediates may include citrulline, ornithine, and carbamyl phosphate. In some embodiments, the other care composition includes citrulline. In some embodiments, the oral care composition includes ornithine. In some embodiments, the oral care composition includes carbamyl phosphate. In other embodiments, the oral care composition includes any combination of citrulline, ornithine, carbamyl phosphate, and/or other intermediates produced by the arginine deiminase system.

[0034] The oral care composition may include the above described intermediates in an effective amount. In some embodiments, the oral care composition includes about 1 mmol/L to about 10 mmol/L intermediate. In other embodiments, the oral care composition includes about 3 mmol/L to about 7 mmol/L intermediate. In other embodiments, the oral care composition includes about 5 mmol/L intermediate.

[0035] The compositions of the invention are intended for topical use in the mouth and so

salts for use in the present invention should be safe for such use, in the amounts and concentrations provided. Suitable salts include salts known in the art to be pharmaceutically acceptable salts are generally considered to be physiologically acceptable in the amounts and concentrations provided. Physiologically acceptable salts include those derived from pharmaceutically acceptable inorganic or organic acids or bases, for example acid addition salts formed by acids which form a physiological acceptable anion, e.g., hydrochloride or bromide salt, and base addition salts formed by bases which form a physiologically acceptable cation, for example those derived from alkali metals such as potassium and sodium or alkaline earth metals such as calcium and magnesium. Physiologically acceptable salts may be obtained using standard procedures known in the art, for example, by reacting a sufficiently basic compound such as an amine with a suitable acid affording a physiologically acceptable anion.

[0036] In various embodiments, the basic amino acid is present in an amount of about 0.5 wt. % to about 20 wt. % of the total composition weight, about 1 wt. % to about 10 wt. % of the total composition weight, for example about 1.5 wt. %, 3.75 wt. %, 5 wt. %, or 7.5 wt. % of the total composition weight.

[0037] RDA: RDA is an abbreviation for radioactive dentin abrasion, a relative measure of abrasivity. Typically, extracted human or cow teeth are irradiated in a neutron flux, mounted in methylmethacrylate (bone glue), stripped of enamel, inserted into a brushing-machine, brushed by American Dental Association (ADA) standards (reference toothbrush, 150g pressure, 1500 strokes, 4-to-1 water-toothpaste slurry). The radioactivity of the rinse water is then measured and recorded. For experimental control, the test is repeated with an ADA reference toothpaste made of calcium pyrophosphate, with this measurement given a value of 100 to calibrate the relative scale.

Fluoride Ion Source

[0038] 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., incorporated herein by reference.

[0039] 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.

[0040] 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., 500 to 2000 ppm, e.g., 1000 – 1600 ppm, e.g., about 1450 ppm. The appropriate level of fluoride will depend on the particular application. A mouthwash, for example, would typically have 100-250 ppm fluoride. A toothpaste for general consumer use would typically have 1000-1500 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.

[0041] 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 one embodiment or about 0.03 wt. % to about 5 wt. %, and in another embodiment about 0.1 wt. % to about 1 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 counter ion in the salt.

Abrasives

[0042] The Compositions of the Invention may comprise a calcium phosphate abrasive, e.g., tricalcium phosphate ($Ca_3(PO_4)_2$), hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$), dicalcium phosphate dihydrate ($CaHPO_4 \cdot 2H_2O$, also sometimes referred to herein as DiCal), or calcium pyrophosphate. Alternatively, calcium carbonate, and in particular precipitated calcium carbonate, may be employed as an abrasive.

[0043] The compositions may include one or more additional abrasives, for example silica abrasives such as precipitated silicas having a mean particle size of up to about 20 microns, such as Zeodent 115®, marketed by J. M. Huber. Other useful abrasives also include sodium metaphosphate, potassium metaphosphate, aluminum silicate, calcined alumina, bentonite or other siliceous materials, or combinations thereof.

[0044] The silica abrasive polishing materials useful herein, as well as the other abrasives, generally have an average particle size ranging about 0.1 – about 30 microns, about 5 - 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, both incorporated herein by reference. 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, incorporated herein by reference.

[0045] 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 about 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 ASTM 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.

[0046] In particular embodiments, the abrasive materials comprise a large fraction of very small particles, e.g., having a d50 less than about 5 microns. For example small particle silica (SPS) having a d50 of about 3 - about 4 microns, for example Sorbosil AC43® (Ineos). Such small particles are particularly useful in formulations targeted at reducing hypersensitivity. The small particle component may be present in combination with a second larger particle abrasive. In certain embodiments, for example, the formulation comprises about 3 to about 8% small particle abrasive e.g., small particle silica and about 10 to about 45% of a conventional abrasive.

[0047] 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 about 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. The abrasive is present in the oral care composition of the present invention at a concentration of about 10 to about 60% by weight, in other embodiment about 20 to about 45% by weight, and in another embodiment about 30 to about 50% by weight.

[0048] In some embodiments the basic amino acid is incorporated into a dentifrice composition having a base formulation comprising calcium carbonate, and in particular precipitated calcium carbonate, as an abrasive. L-arginine and arginine salts such as arginine bicarbonate are themselves distinctly bitter in taste, and in aqueous solution can also impart a fishy taste. Consequently, it was expected that when L-arginine or arginine salts were incorporated into oral care products such as dentifrice formulations at effective concentrations to impart anticavity efficacy and sensitivity relief, typically in an amount of from 2 to 10wt % based on the total weight of the dentifrice formulation, the taste and mouthfeel of the dentifrice formulations would be degraded as compared to the same formulation without the addition of L-arginine or arginine salts.

[0049] However, it has surprisingly been found in accordance with this aspect of the present invention that the addition of L-arginine or arginine salts to a base dentifrice formulation comprising calcium carbonate can provide a significant enhancement of taste and mouthfeel attributes to the dentifrice formulation and to an increase in the overall acceptance of the product to a consumer.

Agents to Increase the Amount of Foaming

[0050] 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.

[0051] 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.

[0052] 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.

[0053] 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. The dosage 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.

Surfactants

[0054] The invention contains 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 cocomo-glyceride sulfate.

ii. higher alkyl sulfates, such as sodium lauryl sulfate,

iii. higher alkyl-ether sulfates, e.g., of formula $CH_3(CH_2)_mCH_2(OCH_2CH_2)_nOSO_3X$, 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 ($CH_3(CH_2)_{10}CH_2(OCH_2CH_2)_2OSO_3Na$).

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.

By "higher alkyl" is meant, e.g., C_{6-30} alkyl. In particular embodiments, the anionic surfactant is selected from sodium lauryl sulfate and sodium ether lauryl sulfate.

[0055] The anionic surfactant is present in an amount which is effective, e.g., greater than about 0.01% by weight of the formulation, but not at a concentration which would be irritating to the oral tissue, e.g., less than about 10%, and optimal concentrations depend on the particular formulation and the particular surfactant. For example, concentrations used or 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%.

[0056] The Compositions of the Invention may optionally contain mixtures of surfactants, comprising anionic surfactants and other surfactants which 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., which are incorporated herein by reference.

[0057] 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. Mixtures of anionic surfactants may also be utilized.

[0058] In another embodiment, cationic surfactants useful in the present invention can be broadly defined as derivatives of aliphatic quaternary ammonium compounds having one long alkyl chain containing about 8 to about 18 carbon atoms such as lauryl trimethylammonium chloride, cetyl pyridinium chloride, cetyl trimethylammonium bromide, di-isobutylphenoxyethyldimethylbenzylammonium chloride, coconut alkyltrimethylammonium nitrite, cetyl pyridinium fluoride, and mixtures thereof.

[0059] Illustrative cationic surfactants are the quaternary ammonium fluorides described in U.S. Pat. No. 3,535,421, to Briner et al., herein incorporated by reference. Certain cationic surfactants can also act as germicides in the compositions.

[0060] Illustrative nonionic surfactants that can be used in the compositions of the invention can be broadly defined as compounds produced by the condensation of alkylene oxide groups (hydrophilic in nature) with an organic hydrophobic compound which may be aliphatic or alkylaromatic in nature. Examples of suitable nonionic surfactants include, but are not limited to, the Pluronics, polyethylene oxide condensates of alkyl phenols, products derived from the condensation of ethylene oxide with the reaction product of propylene oxide and ethylene diamine, ethylene oxide condensates of aliphatic alcohols, long chain tertiary amine oxides, long chain tertiary phosphine oxides, long chain dialkyl sulfoxides and mixtures of such materials.

[0061] In certain embodiments, zwitterionic synthetic surfactants useful in the present invention can be broadly described as derivatives of aliphatic quaternary ammonium, phosphomium, and sulfonium compounds, in which the aliphatic radicals can be straight chain or branched, and wherein one of the aliphatic substituents contains about 8 to about 18 carbon atoms and one contains an anionic water-solubilizing group, e.g., carboxy, sulfonate, sulfate, phosphate or phosphonate. Illustrative examples of the surfactants suited for inclusion into the composition include, but are not limited to, sodium alkyl sulfate, sodium lauroyl sarcosinate, cocoamidopropyl betaine and polysorbate 20, and combinations thereof.

[0062] In a particular embodiment, the Composition of the Invention comprises sodium lauryl sulfate.

[0063] The surfactant or mixtures of compatible surfactants can be present in the compositions of the present invention in about 0.1% to about 5%, in another embodiment about 0.3% to about 3% and in another embodiment about 0.5% to about 2% by weight of the total composition.

Flavoring Agents

[0064] 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.

[0065] The flavoring agent is incorporated in the oral composition at a concentration of about 0.1 to about 5% by weight and about 0.5 to about 1.5% by weight. The dosage of flavoring agent in the individual oral care composition dosage (i.e., a single dose) is about 0.001 to 0.05% by weight and in another embodiment about 0.005 to 0.015 % by weight.

Chelating agents

[0066] The oral care compositions of the invention also may optionally include one or more chelating agents able to complex calcium found in the cell walls of the bacteria. Binding of this calcium weakens the bacterial cell wall and augments bacterial lysis.

[0067] Another group of agents suitable for use as chelating agents in the present invention are the soluble pyrophosphates. The pyrophosphate salts used in the present compositions can be any of the alkali metal pyrophosphate salts. In certain embodiments, salts include tetra alkali metal pyrophosphate, dialkali metal diacid pyrophosphate, trialkali metal monoacid pyrophosphate and mixtures thereof, wherein the alkali metals are sodium or potassium. The salts are useful in both their hydrated and unhydrated forms. An effective amount of pyrophosphate salt useful in the present composition is generally enough to provide at least about 1 wt. % pyrophosphate ions, about 1.5 wt. % to about 6 wt. %, about 3.5 wt. % to about 6 wt. % of such ions.

Polymers

[0068] The oral care compositions of the invention also optionally include one or more polymers, such as polyethylene glycols, polyvinylmethyl ether maleic acid copolymers, 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.

[0069] Particularly when noncationic antibacterial agents or antibacterial agents, e.g., triclosan, are included in any of the dentifrice components, there is also preferably included from about 0.05 to about 5% of an agent which enhances the delivery and retention of the agents to, and retention thereof on oral surfaces. Such agents 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 about 1:4 to about 4:1 copolymers of maleic anhydride or acid with another polymerizable ethylenically unsaturated monomer, preferably methyl vinyl ether/maleic anhydride having a molecular weight (M.W.) of about 30,000 to about 1,000,000, most preferably about 30,000 to about 800,000. These copolymers are available for example as Gantrez, e.g., AN 139 (M.W. 500,000), AN 119 (M.W. 250,000) and preferably S-97 Pharmaceutical Grade (M.W. 700,000) available from ISP Technologies, Inc., Bound Brook, N.J. 08805. The enhancing agents when present are present in amounts ranging from about 0.05 to about 3% by weight.

[0070] Other operative polymers include those such as the 1:1 copolymers of maleic anhydride with ethyl acrylate, hydroxyethyl methacrylate, N-vinyl-2-pyrollidone, 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.

[0071] 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-chlorsorbic, 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.

[0072] 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 acrylamidoalykane 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, incorporated herein by reference.

[0073] Another useful class of polymeric agents includes polyamino acids, particularly those containing proportions of anionic surface-active amino acids such as aspartic acid, glutamic acid and phosphoserine, as disclosed in U.S. Pat. No. 4,866,161 Sikes et al., incorporated herein by reference.

[0074] In preparing oral care compositions, it is sometimes necessary to add some thickening material to provide a desirable consistency or to stabilize or enhance the performance of the formulation. In certain embodiments, the 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 or finely divided silica can 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.

Enzymes

[0075] The oral care compositions of the invention may also optionally include one or more enzymes. Useful enzymes include any of the available proteases, glucanohydrolases, endoglycosidases, amylases, mutanases, lipases and mucinases or compatible mixtures thereof. In certain embodiments, the enzyme is a protease, dextranase, endoglycosidase and mutanase. In another embodiment, the enzyme is papain, endoglycosidase or a mixture of dextranase and mutanase. Additional enzymes suitable for use in the present invention are

disclosed in U.S. Pat. No. 5,000,939 to Dring et al., U.S. Pat. No. 4,992,420; U.S. Pat. No. 4,355,022; U.S. Pat. No. 4,154,815; U.S. Pat. No. 4,058,595; U.S. Pat. No. 3,991,177; and U.S. Pat. No. 3,696,191 all incorporated herein by reference. An enzyme of a mixture of several compatible enzymes in the current invention constitutes about 0.002% to about 2% in one embodiment or about 0.05% to about 1.5% in another embodiment or in yet another embodiment about 0.1% to about 0.5%.

Water

[0076] Water may also be present in the oral compositions of the invention. Water, employed in the preparation of commercial oral compositions should be deionized and free of organic impurities. Water commonly makes up the balance of the compositions and includes about 10% to about 90%, about 20% to about 60% or about 10% to about 30% by weight of the oral compositions. This amount of water includes the free water which is added plus that amount which is introduced with other materials such as with sorbitol or any components of the invention.

Humectants

[0077] 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. The humectant, on a pure humectant basis, generally includes about 15% to about 70% in one embodiment or about 30% to about 65% in another embodiment by weight of the dentifrice composition.

[0078] Suitable humectants include edible polyhydric alcohols such as glycerine, sorbitol, xylitol, propylene glycol as well as other polyols and mixtures of these humectants. Mixtures of glycerine and sorbitol may be used in certain embodiments as the humectant component of the toothpaste compositions herein.

[0079] 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.

Methods of Manufacture

[0080] The compositions of the present invention can be made using methods which are common in the oral product area.

[0081] In one illustrative embodiment, the oral care composition is made by neutralizing or partially neutralizing arginine in a gel phase with an acid, e.g., phosphoric acid, hydrochloric acid or carbonic acid, and mixing to form Premix 1.

[0082] Actives such as, for example, vitamins, CPC, fluoride, abrasives, and any other desired active ingredients are added to Premix 1 and mixed to form Premix 2.

[0083] Where the final product is a toothpaste, a toothpaste base, for example, dicalcium phosphate or silica, is added to Premix 2 and mixed. The final slurry is formed into an oral care product.

Composition Use

[0084] The present invention in its method aspect involves applying to the oral cavity a safe and effective amount of the compositions described herein.

[0085] The compositions and methods according to the invention are useful to a method to protect the teeth by facilitating repair and remineralization, in particular to reduce or inhibit formation of dental caries, reduce or inhibit demineralization and promote remineralization of the teeth, reduce hypersensitivity of the teeth, and reduce, repair or inhibit early enamel lesions, e.g., as detected by quantitative light-induced fluorescence (QLF) or electronic caries monitor (ECM).

[0086] Quantitative Light-induced Fluorescence is a visible light fluorescence that can detect early lesions and longitudinally monitor the progression or regression. Normal teeth fluoresce in visible light; demineralized teeth do not or do so only to a lesser degree. The area of demineralization can be quantified and its progress monitored. Blue laser light is used to make the teeth auto fluoresce. Areas that have lost mineral have lower fluorescence and appear darker in comparison to a sound tooth surface. Software is used to quantify the fluorescence from a white spot or the area/volume associated with the lesion. Generally, subjects with existing white spot lesions are recruited as panelists. The measurements are performed in vivo with real teeth. The lesion area/volume is measured at the beginning of the clinical. The reduction (improvement) in lesion area/volume is measured at the end of 6 months of product use. The data is often reported as a percent improvement versus baseline.

[0087] Electrical Caries Monitoring is a technique used to measure mineral content of the tooth based on electrical resistance. Electrical conductance measurement exploits the fact that the fluid-filled tubules exposed upon demineralization and erosion of the enamel conduct electricity. As a tooth loses mineral, it becomes less resistive to electrical current due to increased porosity. An increase in the conductance of the patient's teeth therefore may indicate demineralization. Generally, studies are conducted of root surfaces with an existing lesion. The measurements are performed in vivo with real teeth. Changes in electrical resistance before and after 6 month treatments are made. In addition, a classical caries score for root surfaces is made using a tactile probe. The hardness is classified on a three point scale: hard, leathery, or soft. In this type of study, typically the results are reported as electrical resistance (higher number is better) for the ECM measurements and an improvement in hardness of the lesion based on the tactile probe score.

[0088] The Compositions of the Invention are thus useful in a method to reduce early lesions of the enamel (as measured by QLF or ECM) relative to a composition lacking effective amounts of fluorine and/or arginine.

[0089] The Compositions of the invention are additionally useful in methods to reduce harmful bacteria in the oral cavity, for example methods to reduce or inhibit gingivitis, reduce levels of acid producing bacteria, to increase relative levels of arginolytic bacteria, inhibit microbial biofilm formation in the oral cavity, raise and/or maintain plaque pH at levels of at least about pH 5.5 following sugar challenge, reduce plaque accumulation, and/or clean the teeth and oral cavity.

[0090] Finally, by increasing the pH in the mouth and discouraging pathogenic bacteria, the Compositions of the Invention are useful to promote healing of sores or cuts in the mouth.

[0091] Enhancing oral health also provides benefits in systemic health, as the oral tissues can be gateways for systemic infections. Good oral health is associated with systemic health, including cardiovascular health. The compositions and methods of the invention provide particular benefits because basic amino acids, especially arginine, are sources of nitrogen which supply NO synthesis pathways and thus enhance microcirculation in the oral tissues. Providing a less acidic oral environment is also helpful in reducing gastric distress and creates an environment less favorable to Heliobacter, which is associated with gastric ulcers. Arginine in particular is required for high expression of specific immune cell receptors, for example T-cell receptors, so that arginine can enhance an effective immune response. The

compositions and methods of the invention are thus useful to enhance systemic health, including cardiovascular health.

[0092] The compositions and methods according to the invention can be incorporated into oral compositions for the care of the mouth and teeth such as toothpastes, transparent pastes, gels, mouth rinses, sprays and chewing gum.

[0093] 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 reference 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. It is understood that when formulations are described, they may be described in terms of their ingredients, as is common in the art, notwithstanding that these ingredients may react with one another in the actual formulation as it is made, stored and used, and such products are intended to be covered by the formulations described.

[0094] The following examples further describe and demonstrate illustrative embodiments within the scope of the present invention. The examples are given solely for illustration and are not to be construed as limitations of this invention as many variations are possible without departing from the spirit and scope thereof. Various modifications of the invention in addition to those shown and described herein should be apparent to those skilled in the art and are intended to fall within the appended claims.

EXAMPLES

Example 1 – Availability and Delivery of Antibacterial in Arginine Formulations

[0095] Formulations are prepared using commercial toothpaste comprising, i.a., 0.3% by weight of triclosan, 0.243% by weight of sodium fluoride, sodium lauryl sulfate, and a copolymer of methyl vinyl ether and maleic anhydride (PVM/MA), to which is added 0, 1%, 3%, and 5% L-arginine hydrochloride (pH 7.0).

[0096] Incorporation of L-arginine in the commercial formulation enhances the amount of soluble triclosan available from the formulation, from about 70% (0% arginine) to about 80% (1% arginine), 85% (3% arginine), and 95% (5% arginine).

[0097] The formulations are tested in vitro in an artificial mouth model designed to measure bacterial attachment to toothpaste-treated hydroxyapatite (HAP) disks over a 24

hour period, generally as described by Gaffar, A. et al. *American Journal of Dentistry*, vol. 3, September 1990, with the modification that the saliva-coated hydroxyapatite disks are treated with the dentifrice slurry before exposure to bacteria. It is shown that the incorporation of L-arginine into the commercial formulation enhances delivery of the triclosan to the disks by about 50%, with uptake at 30 minutes increasing from approximately 40 micrograms triclosan per disk for the control to about 60 micrograms triclosan for the 5% arginine formulation. After 24 hours, the control disks have retained about 10 micrograms per disk, compared to about 20 micrograms for the 5% arginine formulation, a significant enhancement. Similar results are achieved using histidine or lysine in place of arginine.

[0098] This enhanced delivery leads directly to an enhancement of the antibacterial effect of the formulation, with a statistically significant reduction of about 15% in inhibition of growth of *A. viscosus* using the 5% arginine formulation vs. control.

Example 2 – Delivery of Antibacterial in Silica Based Formulations comprising Arginine

[0099] Toothpaste formulations comprising 5% arginine in a silica base are prepared as follows:

Ingredient	Formula I	Formula II	Formula III	Formula IV	Formula V	Formula VI	Formula VII
	Wt%	Wt%	Wt%	Wt%	Wt%	Wt%	Wt%
L-Arginine	5.00	5.00	5.00	5.00	5.00	5.00	5.00
Hydrochloric Acid	-	-	2.00	2.00	2.00	-	-
Silica	21.50	21.50	21.50	23.50	23.50	23.50	23.50
Sodium Fluoride	0.243	0.243	0.243	-	-	-	.0243
Glycerin	20.00	20.00	20.00	20.00	20.00	20.00	20.00
Sorbitol	20.85	20.85	20.85	20.85	20.85	20.85	20.85
Propylene Glycol	0.50	0.50	0.50	-	-	-	2.00
Tetrasodium Pyrophosphate	-	-	-	2.00	2.00	-	2.00
Zinc Lactate, Dihydrate	-	-	-	1.4	-	-	-
Sodium Tripolyphosphate	-	-	-	-	3.00	-	-
Sodium Lauryl Sulfate	1.50	1.50	1.50	1.50	1.50	-	1.50
Poloxomer 407 (Pluronic F-127)	-	-	-	-	-	1.01	-
Cocamidopropyl Betaine (30% solution	-	-	-	1.01	1.01	-	1.01
Hydroxy Ethyl Cellulose	-	-	-	1.50	1.50	1.50	-
Sodium carboxymethyl cellulose	1.10	1.10	1.10	-	-	-	1.10
Carrageenan	0.4	0.4	0.4	-	-	-	0.40
PVM/MA copolymer	2.00	2.00	2.00	-	-	-	-
Sodium Monollurophosphate	-	-	-	0.76	0.76	0.76	-
Flavor	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Sodium Saccharin	0.30	0.30	0.30	0.50	0.50	0.50	0.50
Cationic Compatible Silica	-	-	-	-	-	15.00	-
Abrasive TiO2			0.50	0.50	0.50	0.50	0.50
Sucralose	-	-	-	0.15	0.15	0.15	-
50% Sodium Hydroxide Solution	-	1.20	-	0.10	-	-	-
Triclosan	-	0.30	-	-	-	-	-
Lipophilic agent/Polyphenois	-	-	-	-		-	1.00
Water (To Balance)	QS	QS	Qs	QS	QS	QS	QS

[00100] Triclosan uptake is studied by application of dentifrice slurry on saliva-coated hydroxyapatite disks for a set amount of time at 37 degrees C. The disks are rinsed to remove

excess of dentifrice on the surface. The active that is taken onto the disk is then solubilized and analyzed by HPLC. A commercial toothpaste having a similar formulation to formula II above, comprising, i.a., 0.3% by weight of triclosan, 0.243% by weight of sodium fluoride, sodium lauryl sulfate, and a copolymer of methyl vinyl ether and maleic anhydride, but without arginine, is a positive control. This positive control has a triclosan uptake of 32.7 micrograms per disk vs. an uptake with Formula II of 58.8. The product with arginine thus has an uptake that is 79.8% higher than the commercial formulation.

[00101] In an anti-attachment test, Formula II (0.1845 reduction) outperforms both the positive control (triclosan without arginine, 0.1809 reduction) by a slight, non-significant margin, and Formula 1 (arginine without triclosan, 0.1556 reduction) by a wider margin. In the antibacterial test, Formula II (0.1980 reduction) outperforms the positive control (0.1789 reduction) and Formula I (0.1891 reduction).

Example 3 – Delivery of Antibacterial in Formulations Comprising Precipitated Calcium Carbonate

[00102] Formulations comprising 2% arginine bicarbonate are prepared as follows:

Formula A

RAW MATERIAL	WEIGHT %
Deionized Water	32.420
70% Sorbitol	23.000
Carboxymethyl cellulose	0.940
Xanthan gum	0.210
Sodium saccharin	0.450
Sodium silicate	0.800
Sodium bicarbonate	0.500
Arginine bicarbonate	2.000
Precipitated calcium carbonate	36.000
Sodium monofluorophosphate	0.760
Flavor	1.000
Triclosan	0.300
Sodium lauryl sulfate	1.620
TOTAL	100.000

Formula B

RAW MATERIAL	WEIGHT %
Deionized Water	23.200
70% Sorbitol	23.000
Xylitol	2.500
Carboxymethyl cellulose	0.940
Xanthan gum	0.210
Sodium saccharin	0.450
Sodium silicate	0.800
Sodium bicarbonate	0.500
Arginine bicarbonate	2.000
Precipitated calcium carbonate	42.000
Sodium monofluorophosphate	1.100
Flavor	1.000
Triclosan	0.300
Sodium lauryl sulfate	2.000
TOTAL	100.000

Formula C

RAW MATERIAL	WEIGHT %
Deionized Water	34.420
70% Sorbitol	23.000
Carboxymethyl cellulose	0.940
Xanthan gum	0.210
Sodium saccharin	0.450
Sodium silicate	0.800
Sodium bicarbonate	0.500
Arginine bicarbonate	0.000
Precipitated calcium carbonate	36.000
Sodium monofluorophosphate	0.760
Flavor	1.000
Triclosan	0.300
Sodium lauryl sulfate	1.620
TOTAL	100.000

In the uptake assay described in the preceding examples, Formula A shows 57.86 micrograms of triclosan on the disk vs. 22.88 micrograms for Formula C (control without arginine).

Example 4 – Effect of Sodium Lauryl Sulfate plus Arginine on Bacterial Attachment

[00103] Toothpaste formulations are prepared as follows:

Table 1: Composition of Toothpaste

Ingredients	Arg + SLS Formula 1	Arg w/o SLS Formula 2	SLS w/o Arg Control

Glycerin	22	22	22
Sodium CMC-7MF	1	0.85	1
Tetrasodium pyrophosphate	0.25	0.25	0.25
Water	18.14	15.3	24.94
L-Arginine	5	5	0
Phosphoric Acid	1.8	1.8	0
Sodium MFP	0.76	0.76	0.76
Sodium Saccharin	0.2	0.2	0.2
Dicalcium phosphate dihydrate	48.76	48.76	48.76
Flavor	0.89	0.89	0.89
Sodium Lauryl Sulfate	1.2	0	1.2
Cocamidopropyl betaine	0	1.34	0
Polysorbate 20	0	1.68	0
Pluronic F127	0	1.17	0
Total (%)	100	100	100

Formula 1 containing both arginine and SLS shows a significant anti-attachment effect when tested in vitro. Formula 1 is tested in vitro in the artificial mouth model described above to measure how much bacteria can attach to toothpaste-treated HAP disks over a 24 hour period. The results are compared to a control toothpaste which does not contain arginine. The in vitro test shows a 27% reduction in adhered bacteria for the HAP disks treated with Formula 1 vs. the control sample. Formula 2 containing arginine without SLS only shows a 10% reduction vs. the control indicating that SLS plus arginine combination provides an unexpected advantage in inhibiting bacterial anti-attachment. Formula 1 shows similar results to a positive control toothpaste containing an established anti-attachment agent.

Example 5 - Effect of Sodium Lauryl Sulfate plus Arginine plus PVM/MA on Bacterial Attachment

[00104] A formulation is prepared comprising arginine, sodium lauryl sulfate and an anionic copolymer of methyl vinyl ether and maleic anhydride (PVM/MA - Gantrez S-97):

Ingredient	Weight percent
Demineralized water	q.s.
Sodium saccharin	0.300
Sodium fluoride	0.243
Sorbitol	20.000
Glycerin	15.000
Sodium CMC	1.100
Carrageenan	0.400
Silica (Zeodent 115)	10.000

Silica (Zeodent 165)	3.000
Gantrez S-97	15.000
L-Arginine	5.000
Mint flavor	1.000
Sodium lauryl sulfate	1.500
Propylene glycol	0.500

This formulation shows excellent anti-attachment properties, with over 40% reduction in attachment vs. control.

Example 5 - Mouth rinse formulations

[00105] Mouthwash formulations of the invention are prepared using the following ingredients:

Arginine Rinse with Fluoride, SLS, PMV/MA, and Triclosan

RAW MATERIAL	WEIGHT %
Deionized Water	q.s.
Glycerin	15.000
Sodium methyl cocoyl taurate	0.250
95% Ethanol	6.000
Sodium lauryl sulfate	0.200
Allantoin	0.110
Sodium benzoate	0.100
Sodium salicylate	0.100
Sodium fluoride	0.050
Sodium Saccharin	0.005
Triclosan	0.030
Phosphoric acid 85%	0.120
L-Arginine	0.300
Flavor	0.100
Colorants	0.001
PVM/MA	0.250
TOTAL	100.000
pH	7.0

This formulation is effective to inhibit bacterial attachment.

Example 6 - Dentifrice formulation comprising precipitated calcium carbonate (PCC)

[00106] A panel of consumer testers trained in testing the sensory attributes of dentifrice formulations was subjected to different dentifrice formulations which were used under double-blind consumer testing conditions replicating consumer use of dentifrice formulations.

[00107] The panel was asked to use the dentifrice formulations conventionally and then to

rate various sensory characteristics. For a base dentifrice formulation comprising precipitated calcium carbonate (PCC), the known formulation acted as a placebo control, and corresponding formulations additionally comprising 1, 2, 3 or 5 wt% arginine bicarbonate were also tested. Surprisingly, it was found that the arginine bicarbonate-containing PCC formulations exhibited increases in consumer acceptance for flavor intensity, cooling and ease to foam attributes, and moreover the formulation additionally comprising 2 wt% arginine bicarbonate exhibited increases in overall liking, overall liking of taste, taste while brushing and taste after brushing. In addition, the formulations additionally comprising arginine bicarbonate were perceived as significantly better than the placebo control in all image attributes, including perceived efficacy, mouth/teeth feeling of clean, product suitability, taste and overall product quality.

[00108] In contrast, when formulations having dicalcium phosphate, rather than precipitated calcium carbonate (PCC), as the base were tested, the addition of arginine bicarbonate did not exhibit significantly improved sensory characteristics as compared to the same formulation without the addition of arginine bicarbonate.

[00109] The Example shows that the addition of a basic amino acid such as arginine, in particular as bicarbonate, can surprisingly enhance the sensory characteristics of dentifrice formulations, most particularly having a base formulation of precipitated calcium carbonate (PCC), when used in an oral care composition of the invention.

Example 7 - Basic amino acids other than arginine

[00110] An overnight culture of *S. sanguis* was grown at 37°C in trypticase soy broth (Becton Dickinson, Sparks, MD). The culture was centrifuged at 5,000 rpm for 5 minutes at 1 milliliter at a time into preweighed tubes in order to accumulate approximately 5 milligrams of wet pellet weight. The pellet was then resuspended into 20 millimolar potassium phosphate buffer (JT Baker, Phillipsburg, NJ), pH 4.0, to simulate a stressed environment for the bacterial cell where ammonia would be produced for survival. The final concentration was 5 milligram per milliliter. To this final concentration, a 5 millimolar final concentration of L-arginine, L-citrulline, or L-ornithine was added along with a 0.1% final concentration of sucrose (VWR, West Chester, PA). This mixture was then incubated at 37°C in a shaking water bath for 30 minutes before ammonia production was determined.

[00111] In order to analyze for ammonia, an Ammonia Assay kit was used from Diagnostic Chemicals Limited (Oxford, CT). The intended use of this specific kit is for the

in vitro quantification of ammonia in plasma, but the procedure was modified in order to determine and quantify the ammonia production in plaque and/or bacteria.

[00112] The table below shows the ammonia production values from 6 separate trials using *S. sanguis* at pH 4.0 as described above. The results confirm that the intermediates produced by the arginine deiminase system can be used to produce ammonia for cell survival.

	L-Arginine	**L-Citrulline**	**L-Ornithine**
Trial #	**Ammonia (ppm)**	**Ammonia (ppm)**	**Ammonia (ppm)**
1	0.509	0.185	0.185
2	0.866	0.346	0.260
3	2.20	0.332	0.047
4	1.62	0.194	0.0
5	0.5	0.226	0.181
6	0.679	0.951	0.135
Mean	1.06	0.951	0.134

[00113] The Example shows that basic amino acids other than arginine are effective to produce ammonia within the oral cavity, and thus to increase plaque pH when used in a oral care composition of the invention.

[00114] 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 reference 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. It is understood that when formulations are described, they may be described in terms of their ingredients, as is common in the art, notwithstanding that these ingredients may react with one another in the actual formulation as it is made, stored and used, and such products are intended to be covered by the formulations described.

CLAIMS

1. An oral care composition comprising

a. an effective amount of a basic amino acid, in free or salt form;

b. an anionic surfactant; and

c. an additional agent selected from the combination of an effective amount of an antibacterial agent and an anionic polymer.

2. A composition according claim 1 wherein the basic amino acid is arginine, optionally wherein the basic amino acid is in salt form and selected from arginine phosphate, arginine bicarbonate, and arginine hydrochloride.

3. A composition according to any of the preceding claims wherein the anionic surfactant is selected from sodium lauryl sulfate and sodium laureth sulfate and mixtures thereof.

4. A composition according to any of the preceding claims wherein the anionic surfactant is present in an amount of from 0.01 to 10 weight %, optionally from 0.3 to 4.5 weight%.

5. A composition according to any of the preceding claims comprising and a effective amount of a fluoride source selected from sodium fluoride and sodium monofluorophosphate, optionally comprising a soluble fluoride salt in an amount of from 0.01 to 2 wt% of the total composition weight or to provide 50 to 25,000 ppm by weight of fluoride ions in the total composition weight, further optionally wherein the soluble fluoride salt or source of fluoride ions is selected from sodium fluoride, sodium monofluoropohosphate, and mixtures thereof.

6. A composition according to any of the preceding claims wherein the antibacterial agent is triclosan.

7. A composition according to any of the preceding the preceding claims wherein the anionic polymer is a copolymer of methyl vinyl ether and maleic anhydride.

8. A composition according to any of the preceding claims which is a dentifrice comprising

a. an effective amount of a salt of a basic amino acid selected from arginine bicarbonate, arginine phosphate and arginine hydrochloride;

b. an effective amount of triclosan;

c. an effective amount of a soluble fluoride salt selected from sodium fluoride and sodium monofluophosphate;

d. an anionic surfactant selected from sodium lauryl sulfate and sodium laureth sulfate; and

e. a copolymer of methyl vinyl ether and maleic anhydride.

9. A composition according to any of the preceding claims further comprising xylitol.

10. A composition according to any of the preceding claims comprising an abrasive material, the abrasive material including a small particle fraction comprising at least 5 wt%, optionally from 15 to 30 %, of the total composition weight, wherein the particles of the small particle fraction have a d50 of less than 5 μm, optionally wherein the small particle fraction comprising at least 20 wt% of the total composition weight, further optionally wherein the abrasive material is selected from calcium carbonate, silica, and mixtures thereof.

11. A composition according to any of the preceding claims wherein the radioactive dentin abrasion (RDA) is less than 150.

12. The composition according to any of the preceding claims in the form of a toothpaste further comprising one or more of water, abrasives, surfactants, foaming agents, vitamins, polymers, enzymes, humectants, thickeners, antimicrobial agents, preservatives, flavorings, colorings and/or combinations thereof.

13. The oral composition of any of claims 1 - 12 for use in a method, comprising an effective amount of the oral composition to the oral cavity of a subject in need thereof to

a. reduce or inhibit formation of dental caries,

b. reduce, repair or inhibit early enamel lesions,

c. reduce or inhibit demineralization and promote remineralization of the teeth,

d. reduce hypersensitivity of the teeth,

e. reduce or inhibit gingivitis,

f. promote healing of sores or cuts in the mouth,

g. reduce levels of acid producing bacteria,

h. to increase relative levels of arginolytic bacteria,

i. inhibit bacterial attachment or microbial biofilm formation in the oral cavity,

j. raise and/or maintain plaque pH at levels of at least pH 5.5 following sugar challenge,

k. reduce plaque accumulation,

l. treat dry mouth,

m. whiten teeth,

n. enhance systemic health, including cardiovascular health, e.g., by reducing potential for systemic infection via the oral tissues,

o. reduce erosion of the teeth,

p. immunize the teeth against cariogenic bacteria, and/or

q. clean the teeth and oral cavity.

14. An oral care composition according to any one of the preceding claims wherein the basic amino acid is present in an amount of from 0.1 to 20 wt% of the total composition weight, optionally from 1 to 10 wt% of the total composition weight.

15. An oral care composition according to any of the preceding claims wherein the antibacterial agent is present in an amount of from 0.01 to 5 wt% of the total composition weight, optionally from 0.01 to 1 wt% of the total composition weight.