

BEVERAGE COMPRISING ARGININE

[0001] This application claims the benefit of U.S. Ser. No. 61/027,434 filed February 8, 2008, the contents of which are incorporated herein by reference.

FIELD OF THE INVENTION

[0002] The invention relates to beverages containing arginine, together with calcium, phosphate, and optionally other ions to promote oral health.

BACKGROUND

[0003] Soft drinks containing high levels of sugar are extremely damaging to the teeth. Even diet sodas are damaging due to their high acidity. Sport drinks containing ions to replenish the body following exercise are popular, but tend to be highly sugared, again promoting tooth decay. There is a need for healthy, refreshing drinks which promote rather than damage oral health.

SUMMARY OF THE INVENTION

[0004] 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. Regular use of oral care products comprising arginine, 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. This effect is further enhanced by providing minerals such as calcium, and optionally other minerals such as phosphate and fluoride which promote remineralization of the teeth.

[0005] L-arginine and arginine salts such as arginine-bicarbonate, however, are by themselves distinctly bitter in taste and in solution can also impart a fishy taste. When these ingredients are incorporated in products at effective concentrations to impart anticavity efficacy and sensitivity relief, these ingredients might negatively impact the taste and mouthfeel of the

finished product, particularly when directly compared to a matching formulation without the arginine free base or salt. Surprisingly, the addition of these ingredients results in a significant enhancement of taste and mouthfeel attributes, as well as increase in an overall acceptance of the products.

[0006] The invention thus provides a beverage (Formulation 1.0) comprising an effective amount of

- a. a basic amino acid, e.g., arginine, in free or salt form, e.g., present in an amount of at least 0.1% (by weight of free base),
- b. a calcium salt.

For example, the invention provides

- 1.1. Formulation 1.0 further comprising a phosphate ion source, e.g., a soluble phosphate salt, e.g., potassium phosphate monobasic or dibasic potassium phosphate.
- 1.2. Formulation 1.0 or 1.1 further comprising a potassium ion source, e.g., potassium chloride or potassium phosphate monobasic or dibasic potassium phosphate.
- 1.3. Formulation 1.0, 1.1 or 1.2 further comprising a fluoride source, e.g., a soluble fluoride salt, e.g., sodium fluoride.
- 1.4. Any of the preceding formulations comprising a polyol, e.g., selected from glycerol, sugar alcohols (e.g., sorbitol, xylitol) and combinations thereof.
- 1.5. Any of the preceding formulations comprising xylitol.
- 1.6. Any of the preceding formulations wherein the calcium salt is selected from calcium carbonate, calcium hydroxide, calcium citrate, calcium malate, calcium lactate, calcium chloride, calcium glycerophosphate, calcium formate, and mixtures thereof.
- 1.7. Any of the preceding formulations comprising arginine bicarbonate.
- 1.8. Any of the preceding formulations comprising arginine phosphate.
- 1.9. Any of the preceding formulations comprising an organic acid, e.g., citric acid, malic acid or acetic acid.
- 1.10. Any of the preceding formulations which is carbonated.
- 1.11. Any of the preceding formulations further comprising fruit juice, fruit extract or fruit concentrate.

1.12. Any of the preceding formulations further comprising vitamins (e.g., water soluble vitamins, e.g., B-complex vitamins or ascorbic acid), minerals, antioxidants, and or preservatives.

1.13. Any of the preceding formulations further comprising herbal extracts, e.g., ginseng, green tea, black tea, ginko, guarana, and hoodia.

[0007] The beverages of the invention promote oral and systemic health in a variety of ways, for example, the invention provides method to improve oral health comprising use of the beverages of formulations 1.0-1.13, e.g., by 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 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.

DETAILED DESCRIPTION OF THE INVENTION

[0008] 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 7 or greater.

[0009] Accordingly, basic amino acids include, but are not limited to, arginine, lysine, citrullene, ornithine, creatine, histidine, diaminobutanoic acid, diaminopropionic acid, salts thereof or combinations thereof. In a particular embodiment, the basic amino acids are selected from arginine, citrullene, and ornithine.

[0010] In certain embodiments, the basic amino acid is arginine, for example, L-arginine, or a salt thereof.

[0011] The compositions of the invention are intended for consumption 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.

[0012] The absolute concentration of calcium used in the compositions of the present invention is not critical as this will vary according to the nature and concentration of the acids present. The acid composition may contain organic and/or inorganic acids and may be supplemented with vitamins such as ascorbic acid. The calcium concentration may vary from 0.001 mol. per liter to more than 0.25 mol. per liter, typically from 0.002 mol. per liter to 0.1 mol. per liter, suitably from 0.01 mol. per liter to 0.05 mol. per liter. The calcium may be added in any suitable form, conveniently as a soluble salt such as calcium carbonate, calcium hydroxide, calcium citrate, calcium malate, calcium lactate, calcium chloride, calcium acetate, calcium glycerophosphate or calcium formate or any other salt which minimizes any adverse flavor contribution to the composition.

[0013] Compositions of the invention may be prepared by (i) combining the arginine or basic amino acid with an acid in a Premix 1; (i) mixing an organic acid (e.g., citric acid) with its corresponding calcium salt (e.g., calcium citrate) or another calcium salt to form Premix 2; adding the other ingredients, and combining the Premixes. It may be advantageous to mix the acid with an alkaline calcium salt such as calcium carbonate or calcium hydroxide thereby minimizing the concentration of acid applied to the formulation. The acid can also be mixed with inorganic calcium salts such as calcium chloride. The molar ratio of calcium to acid is 0.3 - 0.55 or 0.4 to 0.55. Most preferably the molar ratio is at least 0.4, and a value of about 0.5 has been found to be especially effective.

[0014] 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 a particular embodiment, the fluoride source is sodium fluoride or sodium monofluorophosphate. Concentrations are generally less than 100 ppm, e.g., 1-25 ppm.

[0015] The products may be unsweetened or sweetened with sugars, sugar alcohols, or intense sweeteners such as saccharine, aspartyl phenyl alanyl methyl ester, or other sweeteners known in the art.

[0016] In a particular embodiment, the product comprises xylitol, which has a sweet taste and is also antibacterial.

[0017] The products may also contain other conventional additives such as sodium benzoate, sorbic acid, sodium metabisulfite, ascorbic acid, flavorings and colorings.

[0018] 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.

Example 1: Formulation comprising Arginine

[0001] Formulations of the invention are prepared from the following ingredients:

Formula A

RAW MATERIAL	WEIGHT %
Deionized Water	96.26815
Xylitol	2.00000
L-Arginine	0.50000
Hydroxyethyl cellulose	0.43000
Flavor	0.40000
Methyl paraben	0.20000
Dibasic potassium phosphate	0.08000
Potassium chloride	0.06200
Potassium phosphate monobasic	0.04300
Calcium chloride dihydrate	0.01000
Magnesium chloride	0.00590
Food colorant	0.00050
Sodium fluoride	0.00045
TOTAL	100.00000

Formula B

RAW MATERIAL	WEIGHT %
Deionized Water	Q.S.
Glycerin	1.000
70% Sorbitol	1.000
Polysorbate 20	0.100
Sodium benzoate	0.010
Calcium chloride	0.600
Sodium Saccharin	0.020
Phosphoric acid 85%	0.080

L-Arginine	0.600
Flavor	0.200
Colorants	0.001
TOTAL	100.000

Formula C

Material	Weight %
Arginine phosphate	0.5
Sodium benzoate	0.01
Apple juice	10
Ascorbic acid	0.03
Malic acid	0.15
Flavoring	0.005
Coloring	0.004
Calcium carbonate	0.093
Sodium hydroxide (to adjust pH)	3.9
Sodium saccharin	0.020
Demineralized water	q.s.

Claims:

1. A beverage comprising an effective amount of
 - a. arginine in free or salt form, in an amount of at least 0.1 % (by weight of free base), and
 - b. a calcium saltwherein the molar ratio of calcium to arginine is 0.3 - 0.55, and wherein the effective amount is an amount effective to promote oral health.
2. The beverage of claim 1 further comprising a phosphate ion source.
3. The beverage of claim 1 or 2 further comprising a potassium ion source.
4. The beverage of any of claims 1 to 3, further comprising a fluoride source.
5. The beverage of any of claims 1 to 4, further comprising a polyol.
6. The beverage of any of claims 1 to 5, further comprising xylitol.
7. The beverage of any of claims 1 to 6, wherein the calcium salt is selected from calcium carbonate, calcium hydroxide, calcium citrate, calcium malate, calcium lactate, calcium chloride, calcium glycerophosphate, calcium formate, and mixtures thereof.
8. The beverage of any of claims 1 to 7, wherein the arginine in free or salt form is arginine bicarbonate.
9. The beverage of any of claims 1 to 8, wherein the arginine in free or salt form is arginine phosphate.
10. The beverage of any of claims 1 to 9, further comprising an organic acid.
11. The beverage of any of claims 1 to 10, which is carbonated.
12. The beverage of any of claims 1 to 11, further comprising fruit juice, fruit extract or fruit concentrate.
13. The beverage of any of claims 1 to 12, further comprising vitamins, minerals, antioxidants, and/or preservatives.
14. Use a beverage of any of claims 1 to 13 in the manufacture of a medicament for
 - a. reducing or inhibiting formation of dental caries,
 - b. reducing, repairing or inhibiting early enamel lesions,
 - c. reducing or inhibiting demineralization and promote remineralization of the teeth,
 - d. reducing hypersensitivity of the teeth,
 - e. reducing or inhibiting gingivitis,
 - f. promoting healing of sores or cuts in the mouth,
 - g. reducing levels of acid producing bacteria,
 - h. increasing relative levels of arginolytic bacteria,
 - i. inhibiting microbial biofilm formation in the oral cavity,

- j. raising and/or maintaining plaque pH at levels of at least pH 5.5 following sugar challenge,
- k. reducing plaque accumulation,
- l. treating dry mouth,
- m. whitening teeth,
- n. enhancing systemic health, including cardiovascular health,
- o. reducing erosion of the teeth,
- p. immunizing the teeth against cariogenic bacteria, and/or
- q. cleaning the teeth and oral cavity;

in a subject in need thereof.