COMPOSITIONS COMPRISING THEOBROMINE TO IMPROVE MECHANICAL STRENGTH OF TEETH

BACKGROUND

1. Field

The present application relates to compositions and methods for preventing dental caries. In particular, the present application relates to aqueous compositions and methods for improving the mechanical strength of teeth.

2. Description of Related Art

Dental caries are one of the most common preventable diseases plaguing humans and non-human animals worldwide. Dental caries (tooth decay, cavity) is caused by bacterial processes which damage hard tooth structure (*e.g.*, enamel, dentin, and cementum). These tooth structures break down progressively, producing holes in teeth (dental caries). Two groups of bacteria — *Streptococcus mutans* and *Lactobacillus* spp. — produce lactic acid in the presence of fermentable carbohydrates such as sucrose, fructose, and glucose, and are largely responsible for initiating caries. Teeth, which are comprised primarily of minerals, are constantly subjected to demineralization and remineralization between teeth and the surrounding saliva. Hydroxylapatite — a crystalline calcium phosphate — is the primary mineral of a tooth's enamel surface and has the general formula $Ca_5(PO_4)_3(OH)$, but is usually written $Ca_{10}(PO_4)_6(OH)_2$ to denote that the crystal unit cell comprises two entities. When the pH at the tooth surface drops below 5.5, demineralization proceeds faster than remineralization (*i.e.* a net loss of hydroxylapatite on the tooth's surface occurs). This loss of mineral structure results in tooth decay. If left untreated, the disease can lead to pain, tooth loss, infection, and, in extreme cases, death.

To prevent dental caries, dental professionals recommend brushing teeth at least twice a day with a fluoride-containing dentifrice, which removes bacterial plaques. Fluoride assists in the prevention of caries by binding to hydroxylapatite surfaces in the tooth enamel, forming fluorapatite and making the enamel more resistant to demineralization (and thus more resistant to decay). Fluoride is also commonly added to municipal water supplies to prevent tooth decay, yet the National Research Council (functioning under the auspices of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine) recently concluded that the levels of fluoride found in municipal water supplies and the levels of fluoride known to cause toxic effects are dangerously close to one another.

There has been little to no innovation in commercial toothpastes since the mid-twentieth century. The active anti-caries ingredient in all commercial toothpastes is either 0.24% sodium

CLAIMS

We claim:

1. Use of a composition comprising an isolated theobromine compound, theobromine salt, polymorphs, or theobromine double salt, at least one source of calcium, and at least one source of phosphate, wherein the pH of said composition is 6.0 to 8.5 in the manufacture of a medicament for treating dental decay in a mammal in need thereof.
2. The use of claim 1, wherein said at least one source of calcium is selected from the group consisting of calcium chloride, calcium carbonate, calcium gluconate, calcium phosphate, and combinations thereof.
3. The use of claim 1, wherein said at least one source of phosphate is selected from the group consisting of potassium dihydrogen phosphate, dipotassium hydrogen phosphate, tripotassium phosphate, sodium dihydrogen phosphate, disodium hydrogen phosphate, trisodium phosphate, and combinations thereof.
4. The use of claim 1, further comprising at least one isotonic agent.
5. The use of claim 4, wherein said isotonic agent is a polyhydric alcohol.
6. The use of claim 5, wherein said polyhydric alcohol is selected from the group consisting of xylitol, sorbitol, mannitol, maltitol, lactitol, isomalt, erythritol, arabitol, glycerol, and combinations thereof.
7. The use of claim 1, wherein said composition further comprises at least one thickener.
8. The use of claim 7, wherein said thickener is selected from the group consisting of methyl cellulose, carboxymethyl cellulose, ethyl cellulose, hydroxypropyl cellulose, and combinations thereof.
9. The use of claim 1, wherein said composition further comprises an antibacterial agent, an antimicrobial agent, or combinations thereof.
10. The use of claim 9, wherein said antibacterial agent is selected from the group consisting of triclosan, hydrogen peroxide, methyl-4-hydroxybenzoate, clove oil, and combinations thereof.
11. The use of claim 1, for enhancing the hardness of at least one tooth, wherein said composition enhances said hardness more than a dentifrice containing 0% to 1.1% of sodium fluoride or 0% to 0.76% sodium monofluorophosphate.
12. The use of claim 11, wherein said composition enhances said hardness more

than a dentifrice containing 0% to 0.5% of sodium fluoride or 0% to 0.76% sodium monofluorophosphate.

13. The use of claim 11, wherein said composition enhances said hardness more than a dentifrice containing 0% to 0.25% of sodium fluoride or 0% to 0.76% sodium monofluorophosphate.

14. The use of claim 11, wherein said composition enhances said hardness more than a dentifrice containing 0% to 0.15% of sodium fluoride or 0% to 0.76% sodium monofluorophosphate.

15. Use of a composition comprising an isolated theobromine compound, theobromine salt, or theobromine double salt, at least one source of calcium, and at least one source of phosphate, wherein the pH of said composition is 6.0 to 8.5 in the manufacture of a medicament for enhancing the indentation hardness of at least one tooth to said mammal.

16. The use of claim 15, wherein said at least one source of calcium is selected from the group consisting of calcium chloride, calcium carbonate, calcium gluconate, calcium phosphate, and combinations thereof.

17. The use of claim 15, wherein said at least one source of phosphate is selected from the group consisting of potassium dihydrogen phosphate, dipotassium hydrogen phosphate, tripotassium phosphate, sodium dihydrogen phosphate, disodium hydrogen phosphate, trisodium phosphate, and combinations thereof.

18. The use of claim 15, further comprising at least one isotonic agent.

19. The use of claim 18, wherein said isotonic agent is a polyhydric alcohol.

20. The use of claim 19, wherein said polyhydric alcohol is selected from the group consisting of xylitol, sorbitol, mannitol, maltitol, lactitol, isomalt, erythritol, arabitol, glycerol, and combinations thereof.

21. The use of claim 15, wherein said composition further comprises at least one thickener.

22. The use of claim 21, wherein said thickener is selected from the group consisting of methyl cellulose, carboxymethyl cellulose, ethyl cellulose, hydroxypropyl cellulose, and combinations thereof.

23. The use of claim 15, wherein said composition further comprises an antibacterial agent, an antimicrobial agent, or combinations thereof.

24. The use of claim 23, wherein said antibacterial agent is selected from the group consisting of triclosan, hydrogen peroxide, methyl-4-hydroxybenzoate, clove oil, and

combinations thereof.

25. The use of claim 15, for enhancing the hardness of at least one tooth, wherein said composition enhances said hardness more than a dentifrice containing 0% to 1.1% of either sodium fluoride or sodium monofluorophosphate.

26. The use of claim 25, wherein said composition enhances said hardness more than a dentifrice containing 0% to 0.5% of sodium fluoride or 0% to 0.76% sodium monofluorophosphate.

27. The use of claim 25, wherein said composition enhances said hardness more than adentifrice containing 0% to 0.25% of sodium fluoride or 0% to 0.76% sodium monofluorophosphate.

28. The use of claim 25, wherein said composition enhances said hardness more than a dentifrice containing 0% to 0.15% of sodium fluoride or 0% to 0.76% sodium monofluorophosphate.

29. The use of claim 25, wherein said enhancing further comprises deposition of new hydroxylapatite and/or calcium phosphate onto said tooth.

METHODS AND COMPOSITIONS TO IMPROVE MECHANICAL RESISTANCE OF TEETH

BACKGROUND

1. Field

The present application relates to compositions and methods for preventing dental caries. In particular, the present application relates to aqueous compositions and methods for improving the mechanical strength of teeth.

2. Description of Related Art

Dental caries are one of the most common preventable diseases plaguing humans and non-human animals worldwide. Dental caries (tooth decay, cavity) is caused by bacterial processes which damage hard tooth structure (*e.g.*, enamel, dentin, and cementum). These tooth structures break down progressively, producing holes in teeth (dental caries). Two groups of bacteria — *Streptococcus mutans* and *Lactobacillus* spp. — produce lactic acid in the presence of fermentable carbohydrates such as sucrose, fructose, and glucose, and are largely responsible for initiating caries. Teeth, which are comprised primarily of minerals, are constantly subjected to demineralization and remineralization between teeth and the surrounding saliva. Hydroxylapatite — a crystalline calcium phosphate — is the primary mineral of a tooth's enamel surface and has the general formula $Ca_5(PO_4)_3(OH)$, but is usually written $Ca_{10}(PO_4)_6(OH)_2$ to denote that the crystal unit cell comprises two entities. When the pH at the tooth surface drops below 5.5, demineralization proceeds faster than remineralization (*i.e.* a net loss of hydroxylapatite on the tooth's surface occurs). This loss of mineral structure results in tooth decay. If left untreated, the disease can lead to pain, tooth loss, infection, and, in extreme cases, death.

To prevent dental caries, dental professionals recommend brushing teeth at least twice a day with a fluoride-containing dentifrice, which removes bacterial plaques. Fluoride assists in the prevention of caries by binding to hydroxylapatite surfaces in the tooth enamel, forming fluorapatite and making the enamel more resistant to demineralization (and thus more resistant to decay). Fluoride is also commonly added to municipal water supplies to prevent tooth decay, yet the National Research Council (functioning under the auspices of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine) recently concluded that the levels of fluoride found in municipal water supplies and the levels of fluoride known to cause toxic effects are dangerously close to one another.

There has been little to no innovation in commercial toothpastes since the mid-twentieth century. The active anti-caries ingredient in all commercial toothpastes is either 0.24% sodium

CLAIMS

We claim:

1. A composition, said composition comprising:
    a) an isolated theobromine compound, or a salt or double salt thereof;
    b) at least one source of calcium;
    c) at least one source of phosphate; and
    d) a pH of about 6.0 to about 8.5.
2. The composition of claim 1, wherein said at least one source of calcium is selected from the group consisting of calcium chloride, calcium carbonate, calcium gluconate, calcium phosphate, and combinations thereof.
3. The composition of claim 1, wherein said at least one source of phosphate is selected from the group consisting of potassium dihydrogen phosphate, dipotassium hydrogen phosphate, tripotassium phosphate, sodium dihydrogen phosphate, disodium hydrogen phosphate, trisodium phosphate, and combinations thereof.
4. The composition of claim 1, further comprising at least one isotonic agent.
5. The composition of claim 4, wherein said isotonic agent is a polyhydric alcohol.
6. The composition of claim 5, wherein said polyhydric alcohol is selected from the group consisting of xylitol, sorbitol, mannitol, maltitol, lactitol, isomalt, erythritol, arabitol, glycerol, and combinations thereof.
7. The composition of claim 1, further comprising at least one thickener.
8. The composition of claim 7, wherein said thickener is selected from the group consisting of methyl cellulose, carboxymethyl cellulose, ethyl cellulose, hydroxypropyl cellulose, and combinations thereof.
9. The composition of claim 1, further comprising an antibacterial agent, an antimicrobial agent, or combinations thereof.
10. The composition of claim 9, wherein said antibacterial agent is selected from the group consisting of triclosan, hydrogen peroxide, methyl-4-hydroxybenzoate, clove oil, and combinations thereof.
11. The composition of claim 1, for enhancing the hardness of at least one tooth, wherein said composition enhances said hardness more than a dentifrice containing 0% to about 1.1% of sodium fluoride or 0% to about 0.76% sodium monofluorophosphate.

12. The composition of claim 11, wherein said composition enhances said hardness more than a dentifrice containing 0% to about 0.5% of sodium fluoride or 0% to about 0.76% sodium monofluorophosphate.

13. The composition of claim 11, wherein said composition enhances said hardness more than a dentifrice containing 0% to about 0.25% of sodium fluoride or 0% to about 0.76% sodium monofluorophosphate.

14. The composition of claim 11, wherein said composition enhances said hardness more than a dentifrice containing 0% to about 0.15% of sodium fluoride or 0% to about 0.76% sodium monofluorophosphate.

15. Use of a composition comprising an isolated theobromine compound, theobromine salt, polymorphs, or theobromine double salt, at least one source of calcium, and at least one source of phosphate, wherein the pH of said composition is about 6.0 to about 8.5 in the manufacture of a medicament for treating dental decay in a mammal in need thereof.

16. The use of claim 15, wherein said at least one source of calcium is selected from the group consisting of calcium chloride, calcium carbonate, calcium gluconate, calcium phosphate, and combinations thereof.

17. The use of claim 15, wherein said at least one source of phosphate is selected from the group consisting of potassium dihydrogen phosphate, dipotassium hydrogen phosphate, tripotassium phosphate, sodium dihydrogen phosphate, disodium hydrogen phosphate, trisodium phosphate, and combinations thereof.

18. The use of claim 15, further comprising at least one isotonic agent.

19. The use of claim 18, wherein said isotonic agent is a polyhydric alcohol.

20. The use of claim 19, wherein said polyhydric alcohol is selected from the group consisting of xylitol, sorbitol, mannitol, maltitol, lactitol, isomalt, erythritol, arabitol, glycerol, and combinations thereof.

21. The use of claim 15, wherein said composition further comprises at least one thickener.

22. The use of claim 21, wherein said thickener is selected from the group consisting of methyl cellulose, carboxymethyl cellulose, ethyl cellulose, hydroxypropyl cellulose, and combinations thereof.

23. The use of claim 15, wherein said composition further comprises an antibacterial agent, an antimicrobial agent, or combinations thereof.

24. The use of claim 23, wherein said antibacterial agent is selected from the group consisting of triclosan, hydrogen peroxide, methyl-4-hydroxybenzoate, clove oil, and combinations thereof.

25. The use of claim 15, for enhancing the hardness of at least one tooth, wherein said composition enhances said hardness more than a dentifrice containing 0% to about 1.1% of sodium fluoride or 0% to about 0.76% sodium monofluorophosphate.

26. The use of claim 25, wherein said composition enhances said hardness more than a dentifrice containing 0% to about 0.5% of sodium fluoride or 0% to about 0.76% sodium monofluorophosphate.

27. The use of claim 25, wherein said composition enhances said hardness more than a dentifrice containing 0% to about 0.25% of sodium fluoride or 0% to about 0.76% sodium monofluorophosphate.

28. The use of claim 25, wherein said composition enhances said hardness more than a dentifrice containing 0% to about 0.15% of sodium fluoride or 0% to about 0.76% sodium monofluorophosphate.

29. Use of a composition comprising an isolated theobromine compound, theobromine salt, or theobromine double salt, at least one source of calcium, and at least one source of phosphate, wherein the pH of said composition is about 6.0 to about 8.5 in the manufacture of a medicament for enhancing the indentation hardness of at least one tooth to said mammal.

30. The use of claim 29, wherein said at least one source of calcium is selected from

the group consisting of calcium chloride, calcium carbonate, calcium gluconate, calcium phosphate, and combinations thereof.

31. The use of claim 29, wherein said at least one source of phosphate is selected from the group consisting of potassium dihydrogen phosphate, dipotassium hydrogen phosphate, tripotassium phosphate, sodium dihydrogen phosphate, disodium hydrogen phosphate, trisodium phosphate, and combinations thereof.

32. The use of claim 29, further comprising at least one isotonic agent.

33. The use of claim 32, wherein said isotonic agent is a polyhydric alcohol.

34. The use of claim 33, wherein said polyhydric alcohol is selected from the group consisting of xylitol, sorbitol, mannitol, maltitol, lactitol, isomalt, erythritol, arabitol, glycerol, and combinations thereof.

35. The use of claim 29, wherein said composition further comprises at least one thickener.

36. The use of claim 35, wherein said thickener is selected from the group consisting of methyl cellulose, carboxymethyl cellulose, ethyl cellulose, hydroxypropyl cellulose, and combinations thereof.

37. The use of claim 29, wherein said composition further comprises an antibacterial agent, an antimicrobial agent, or combinations thereof.

38. The use of claim 37, wherein said antibacterial agent is selected from the group consisting of triclosan, hydrogen peroxide, methyl-4-hydroxybenzoate, clove oil, and combinations thereof.

39. The use of claim 29, for enhancing the hardness of at least one tooth, wherein said composition enhances said hardness more than a dentifrice containing 0% to about 1.1% of either sodium fluoride or sodium monofluorophosphate.

40. The use of claim 39, wherein said composition enhances said hardness more than a dentifrice containing 0% to about 0.5% of sodium fluoride or 0% to about 0.76%

sodium monofluorophosphate.

41. The use of claim 39, wherein said composition enhances said hardness more than adentifrice containing 0% to about 0.25% of sodium fluoride or 0% to about 0.76% sodium monofluorophosphate.

42. The use of claim 39, wherein said composition enhances said hardness more than a dentifrice containing 0% to about 0.15% of sodium fluoride or 0% to about 0.76% sodium monofluorophosphate.

43. The use of claim 29, wherein said enhancing further comprises deposition of new hydroxylapatite and/or calcium phosphate onto said tooth.