ALCOHOL-FREE MOUTHWASH

FIELD OF THE INVENTION

[0001] The present invention relates to novel liquid alcohol-free oral care compositions comprising cetylpyridinium chloride.

BACKGROUND OF THE INVENTION

[0002] Conventional mouthwash compositions frequently contain ethanol, up to 27% volume, as a preservative and antimicrobial agent. In some individuals, alcohol may exacerbate xerostomia (dry mouth), which in turn can cause halitosis and significant tooth decay, as the protective effect of saliva's remineralizing the enamel is reduced. Xerostomia also makes the mucosa and periodontal tissue of the mouth more vulnerable to infection and increases the risk of gingivitis. Mouthwash comprising high levels of alcohol also may be undesirable for use by alcoholics, children, and members of certain religious faiths, and some consumers may object to the burning sensation of relatively high alcohol compositions.

[0003] Cetylpyridinium chloride (CPC) is a cationic quaternary ammonium compound frequently used in addition to or in place of ethanol as an antiseptic and preservative in mouthwashes, toothpastes, lozenges, throat sprays, breath sprays, and nasal sprays. At effective concentrations, e.g. ca. 0.07%, CPC kills bacteria and other microorganisms and has been shown to be effective in preventing dental plaque and reducing gingivitis. It is believed to kill bacteria by binding to the negatively charged phosphates of the bacterial cell membrane. Formulating CPC presents challenges, however, because of its bitter taste and its incompatibility with many composition excipients. Ethanol can be helpful in such compositions as it acts as a solubilizer for many ingredients and is a flavor enhancer, but a noted above, there are disadvantages to oral care products comprising ethanol.

[0004] There is a need for ethanol-free liquid oral care compositions having an acceptable taste.

BRIEF SUMMARY OF THE INVENTION

[0005] The invention provides ethanol-free liquid oral care compositions comprising CPC that do not have an unacceptably bitter taste. This is accomplished by admixing relatively insoluble flavoring oils with the CPC in a particular ratio. For example, the invention provides a liquid oral care composition which is substantially free of ethanol, comprising (i) an antimicrobially

effective amount of cetyl pyridinium chloride (CPC) and (ii) one or more flavoring oils which are substantially insoluble in water at room temperature, wherein the ratio of the CPC to the one or more flavoring oils is from 1:1.5 to 1:2.5. Without intending to be bound by theory, it is believed, that at optimal concentrations, the CPC and the one or more flavoring oils spontaneously or with gentle mixing can form a stable micelle or a water-in-oil microemulsion at room temperature in the presence of water, which helps mask the bitter taste of the CPC without affecting its efficacy as an antibacterial agent, and at the same time, the surfactant properties of the CPC allow elevated levels of poorly soluble oils which themselves may have antibacterial properties.

[0006] Further areas of applicability of the present invention will become apparent from the detailed description provided hereinafter. It should be understood that the detailed description and specific examples, while indicating the preferred embodiment of the invention, are intended for purposes of illustration only and are not intended to limit the scope of the invention.

DETAILED DESCRIPTION OF THE INVENTION

[0007] In one embodiment, the invention provides a liquid oral care composition (Composition 1) which is substantially free of ethanol, e.g., less than 5% ethanol, comprising (i) an antimicrobially effective amount of cetyl pyridinium chloride (CPC), and (ii) one or more flavoring oils which are substantially insoluble. E.g., less than 1% soluble, in water at room temperature, wherein the ratio of the CPC to the one or more flavoring oils is from 1:1.5 to 1:2.5. For example, the invention provides

1.1. The liquid oral care composition of Composition 1 wherein the ratio of the CPC to the one or more flavoring oils is 1:1.6 to 1:1.9.

1.2. The liquid oral care composition of Composition 1 or 1.1 wherein the CPC and the one or more flavoring oils form a micelle or a water-in-oil microemulsion in aqueous media at room temperature.

1.3. The liquid oral care composition of any of the foregoing Compositions wherein the one or more flavoring oils comprise menthol.

1.4. The liquid oral care composition of any of the foregoing Compositions wherein the one or more flavoring oils comprise menthol, spearmint oil, peppermint oil, or combinations of any of these.

1.5. The liquid oral care composition of any of the foregoing Compositions wherein the one of more flavoring oils are selected from one or more of menthol, spearmint oil, peppermint oil, carvone, methyl salicylate, anethole, thymol, eugenol, coolants, cinnamic aldehydes, and mixtures thereof.

1.6. The liquid oral care composition of any of the foregoing Compositions wherein the one or more flavoring oils comprise a combination of menthol, spearmint oil and peppermint oil in a ratio to CPC as follows:

1 part CPC :

0.3 – 0.9 parts menthol :

0.4 – 1.2 parts spearmint oil :

0.1 – 0.5 parts peppermint oil.

1.7. The liquid oral care composition of any of the foregoing Compositions that is substantially free of ethanol and that comprises

an antimicrobially effective amount of cetyl pyridinium chloride (e.g., 0.05 – 0.1%/weight, e.g., 0.07-0.08%, about 0.075% by weight), and

an effective amount of a flavoring component (e.g., 0.05 – 0.3%, e.g., 0.1 – 0.2%, e.g., about 0.12% by weight of total composition), the flavoring component comprising

menthol, e.g. in an amount of at least 15%, e.g., 15-25%, e.g. about 20% by weight of flavoring component;

peppermint oil (e.g., natural peppermint oil, synthetic peppermint oil, cornmint oil or mixtures thereof), e.g., in an amount of at least 10%, e.g., 10-20%, e.g., about 15% by weight of flavoring component;

spearmint oil, e.g., in an amount of 30-55%, e.g., 40-50%, about 45% by weight of flavoring component;

1.8. The liquid oral care composition of any of the foregoing Compositions (e.g. mouthwashes, toothpastes, throat sprays, and breath sprays) being substantially free of ethanol and comprising an antimicrobially effective amount of a CPC and flavorants in the following ratio:

1 part CPC :

0.3 – 0.9, e.g., 0.5-0.7 parts menthol :

0.4 – 1.2, e.g., 0.5 – 0.8 parts spearmint oil :
0.1 – 0.5, e.g., 0.2 – 0.4 parts peppermint oil;
and optionally further ingredients, e.g., further comprising one or more of additional flavorants, e.g., comprising one or more of anethole (e.g., trans-anethole), thymol, methyl salicylate, coolants (for example n-ethyl-p-menthane-3-carboxamide, Optacool®), cinnamic aldehydes and mixtures thereof;
additional preservatives, e.g, paraben preservatives, for example methyl p-hydroxybenzoate, propyl p-hydroxybenzoate, and mixtures thereof;
non-caloric sweeteners, e.g., comprising saccharin, sugar alcohols (e.g., sorbitol), or mixtures thereof;
humectants, e.g., comprising propylene glycol, glycerin or mixtures thereof;
non-ionic surfactants, e.g., poloxamers, e.g., poloxamer 470;
a fluoride ion source, e.g, sodium fluoride; and
water.

1.9. The liquid oral care composition of any of the foregoing Compositions in the form of a mouthwash;

1.10. The liquid oral care composition of any of the foregoing Compositions comprising CPC and a flavor component comprising flavorants in a ratio of CPC and flavorants by weight is about 1 part CPC : about 0.3 parts menthol : about 0.7 parts spearmint oil : about 0.24 parts peppermint oil; wherein the composition may optionally comprise coolants and/or sweeteners in addition to the flavor component.

1.11. The liquid oral care composition of any of the foregoing Compositions wherein the flavor component comprises by weight of flavor component about 20% menthol, about 45% spearmint oil and about 15% peppermint oil;

1.12. The liquid oral care composition of any of the foregoing Compositions comprising L-menthol;

1.13. The liquid oral care composition of any of the foregoing Compositions comprising menthol in addition to the menthol in the flavoring component, e.g.,

0.01-0.04, e.g., about 0.02% menthol by weight of the total composition, in addition to the menthol in the flavoring component;

1.14. A composition according to any of the preceding compositions comprising 0.05-0.07% total menthol, e.g., including added menthol and menthol from peppermint oil and spearmint oil

1.15. A composition according to any of the preceding embodiments wherein the flavoring component further comprises an anethole, e.g., trans-anethole, in an amount of 1-10%, e.g., 2-6%, e.g., about 4% by weight of flavoring component; or 0.001-0.01%, e.g., 0.002-0.006% e.g., about 0.004% by weight of the total composition;

1.16. A composition according to any of the preceding embodiments which is an aqueous solution, water-in-oil emulsion, water-in-oil microemulsion, or micellar system;

1.17. A composition according to any of the preceding embodiments which is a water-in-oil microemulsion;

1.18. A composition according to any of the preceding embodiments which is a micellar system;

1.19. A composition according to any of the preceding embodiments further comprising additional flavorants, e.g., comprising one or more of anethole (e.g., trans-anethole), thymol, coolants (for example comprising menthol, n-ethyl-p-menthane-3-carboxamide, and combinations thereof), cinnamic aldehydes and mixtures thereof, for example coolant mixtures available commercially, e.g. Optacool®(Symrise).;

1.20. A composition according to any of the preceding embodiments further comprising additional preservatives, e.g, paraben preservatives, for example methyl p-hydroxybenzoate, propyl p-hydroxybenzoate, and mixtures thereof;

1.21. A composition according to any of the preceding embodiments further comprising non-caloric sweeteners, e.g., comprising saccharin, sugar alcohols (e.g., sorbitol), or mixtures thereof;

1.22. A composition according to any of the preceding embodiments further comprising humectants, e.g., comprising propylene glycol, glycerin or mixtures thereof;

1.23. A composition according to any of the preceding embodiments comprising water, colorant, sodium saccharide, sodium fluoride, CPC, poloxamer, e.g., Pluronic F-127, sorbitol, glycerin, propylene glycol, parabens, and menthol, wherein the composition is substantially clear.

1.24. A composition according to any of the preceding embodiments further comprising non-ionic surfactants, e.g., poloxamers, e.g., poloxamer 470;

1.25. A composition according to any of the preceding embodiments further comprising a fluoride ion source, e.g, sodium fluoride;

1.26. A composition according to any of the preceding embodiments which is an aqueous solution, water-in-oil emulsion, or water-in-oil microemulsion;

1.27. A composition according to any of the foregoing embodiments comprising the following ingredients, by weight:

i)	sorbitol	4-7%,
ii)	humectant, e.g, glycerin, propylene glycol and combinations thereof	12-18%
iii)	sodium fluoride	0.04 – 0.06%
iv)	cetylpyridinium chloride	0.05 – 0.1%
v)	sodium saccharin	0.01- 0.03%
vi)	polaxamer 407	0.3 - 0.5%
vii)	flavoring component	0.05 – 0.5%, e.g., 0.1 – 0.3%
viii)	menthol / coolant (in addition to flavoring component)	0.02-0.06%
ix)	dye	0.0 – 0.01%
x)	parabens	0.02 – 0.06%
xi)	water	75 - 85%

wherein the flavor component comprises 85-100% insoluble flavoring oils.

1.28. A composition according to any of the preceding embodiments comprising the following ingredients, by weight:

sorbitol	3-5%, e.g., about 4%
glycerin	6-9%, e.g., about 7.5%

propylene glycol	6-8%, e.g., about 7%
sodium fluoride	0.04 – 0.06%, e.g., about 0.05%
cetylpyridinium chloride	0.05 – 0.1%, e.g., about 0.075%
sodium saccharin	0.01- 0.03%, e.g., about 0.2%
polaxamer 407	0.3 - 0.5%, e.g., about 0.4%
flavoring component	0.05 – 0.5, e.g., 0.1 – 0.3%, e.g., about 0.12%
menthol / coolant (in addition to flavoring component)	0.02-0.06%, e.g., about 0.045%
dye	0.0 – 0.01, e.g., about 0.001%
parabens, e.g., (about 3:1 methyl p-hydroxybenzoate : propyl –p-hydroxybenzoate)	0.02 – 0.06%, e.g., about 0.04%
water	75 - 85%, e.g., balance

wherein the flavor component comprises:

L-menthol	15-25%, e.g. about 20%
N-ethyl-p-menthane-3-carboxamide	1-3%, e.g., about 2%
trans-anethole	2-6%, e.g., about 4%
eugenol	0.1-0.3%, e.g., about 0.2%
Peppermint oil (e.g., 2:1 cornmint oil : synthetic peppermint oil)	10-20%, e.g., about 15%
thymol	0.2-0.6%, e.g., about 0.4%
methyl salicylate	10-15%, e.g., about 13%
cinnamic aldehydes	0.1-0.3%, e.g., about 0.2%
spearmint oil	35-55%, e.g., about 45%

[0008] The invention further provides methods of prophylaxis and/or treatment of a disease or condition selected from one or more of dry mouth, halitosis, gingivitis, tooth decay, and cavities, comprising administering an effective amount of a composition as hereinbefore described, e.g. any of Compositions 1, 1.1, et seq., to a subject in need thereof.

[0009] The invention further provides the use of cetyl pyridinium chloride (CPC) and one or more flavoring oils which are substantially insoluble in water at room temperature, in a ratio of the CPC to the one or more flavoring oils from 1:1.5 to 1:2.5, in the manufacture of a liquid oral care composition, e.g. any of Compositions 1, 1.1, et seq., for prophylaxis and/or treatment of a disease or condition selected from one or more of dry mouth, halitosis, gingivitis, tooth decay, and cavities.

[0010] The invention further provides a method of making a composition, e.g. any of Compositions 1, 1.1, et seq., comprising adding flavoring oils to an aqueous solution comprising cetylpyridinium chloride and mixing until the composition is clear, e.g., a method comprising adding colorant to water and mixing, then adding sodium saccharide, sodium fluoride and CPC and mixing, then adding a poloxamer, e.g., Pluronic F-127 and mixing, then adding add sorbitol and glycerin and mixing, and then adding a mixture of propylene glycol, parabens, and menthol and other flavorings, and mixing until the composition is clear.

[0011] As used throughout, ranges are used as shorthand for describing each and every value that is within the range. Any value within the range can be selected as the terminus of the range. In addition, all references cited herein are hereby incorporated by referenced in their entireties. In the event of a conflict in a definition in the present disclosure and that of a cited reference, the present disclosure controls.

[0012] Unless otherwise specified, all percentages and amounts expressed herein and elsewhere in the specification should be understood to refer to percentages by weight. The amounts given are based on the active weight of the material.

Example 1 – Comparative compositions

[0013] Compositions are prepared with different flavoring oils as follows:

Table 1 – Mouthrinse compositions

Ingredient	Formula A (%)	Formula B (%)
Sorbitol (70% solution)	5.5	5.5

Glycerin	7.5	7.5`
Propylene glycol	7.0	7.0
Sodium fluoride	0.05	0.05
Cetylpyridinium chloride	0.075	0.075
Sodium saccharin	0.022	0.022
Poloxamer 407`	0.4	0.4
Flavor A	0.12	--
Flavor B	--	0.12
Menthol	0.02	0.02
Coolant blend (Optacool ®)	0.025	0.025
Dye	0.001	0.001
Methyl-*p*-hydroxybenzoate	0.03	0.03
Propyl- *p*-hydroxybenzoate	0.01	0.01
Water	balance	balance

Table 2 – Flavoring components

Ingredient	Flavor A (%)	Flavor B (%)
L-menthol	20	15
North American peppermint oil	--	9
North American spearmint oil	45	56
Synthetic peppermint oil	5	--
Cornmint oil	10	--
N-ethyl-*p*-menthane-3-carboxamide	2	2
Trans-anethole	4	4
Eugenol	0.2	0.2
Thymol	0.4	0.4
Cinnamic aldehydes	0.2	0.2
Methyl salicylate	13.2	13.2

Example 2 – Consumer testing

[0014] The compositions of the previous example were tested with consumers to measure flavor liking and purchase intent.

Table 3 – Consumer test results

	Formula A	Formula B
Purchase Intent (Definitely would buy – Top Box)	85%	76%
Has taste I like	87%	80%
Gives long-lasting freshness	85%	74%
Intensity of flavor – Like it a lot	87%	74%

[0015] Generally, the more acceptable composition, Formula A, had higher levels of menthol and peppermint oil relative to spearmint oil. Spearmint oil and peppermint oil differ, *inter alia*, in that peppermint oil has higher amounts of menthol. This difference, coupled with the higher level of added menthol, means that Formula A had significantly more menthol than Formula B.

[0016] Without being bound by theory, it is hypothesized that the relatively higher levels of poorly soluble menthol in Formula A permit formation of a spontaneous microemulsion or micellar system incorporating the CPC, reducing the perception of bitter taste from the CPC. At the same time, the CPC allows the composition to contain higher levels of poorly soluble oils such as menthol, which themselves have antibacterial properties, thereby enhancing the efficacy of the composition.

Example 3 – Flavor refinement

[0017] Further flavorings were tested in the above mouthwash composition, confirming that CPC compositions comprising higher levels of insoluble or poorly soluble oils are preferred by consumers. Mouthwashes with the following flavoring compositions were consumer tested (ingredients given as percent by weight of flavoring):

Table 3 – Flavoring components

Ingredient	Flavor C	Flavor D	Flavor E	Flavor F
L-menthol	20	43	18	14
N-ethyl-*p*-menthane-3-carboxamide	7	1	2	1.6

2-isopropyl-N,2,3-trimethylbutyramide	7			
Trans-anethole	5	6	2	1.6
Eugenol	1	1		
Optacool Special C flavor	10	7		
Optamint flavor	20	12		
BrightStar 7.0	20			
Cornmint oil	10	13		
Methyl salicylate			14	14.2
Peppermint flavor			3	2.4
Spearmint mixture			12	9.6
L-carvone			33	30
Soft mint combo			16	13.8
Artificial alcohol replacer				12
Total percent poorly soluble oils other than added menthol	66	37	80	71.6
Total percent poorly soluble oils including added menthol	86	80	98	85.6

[0018] Mouthrinse with flavoring C is compared to mouthrinse with flavoring D, and mouthrinse with flavoring E is compared to mouthrinse with flavoring F. Consumers show a marked preference for C over D and for E over F, confirming that the products having higher levels of insoluble or poorly soluble oils are preferred, and that there is a preferred range for menthol in the flavoring, e.g., greater than 15% but less than 43%, preferably about 18-20%, in addition to the menthol present in the mint oil and in the base formulation. In the base formulations used, which comprise 0.12% flavor and 0.02% added menthol, this corresponds to a total of 0.042-0.044 % menthol in the formulation, plus the menthol present in the mint oils. The overall ratio of CPC (0.075%) to insoluble oils (0.12 – 0.14%) in the formulation would thus be from 1:1.6 to 1:1.9.

CLAIMS

1. A liquid oral care composition which is substantially free of ethanol, comprising (i) an antimicrobially effective amount of cetyl pyridinium chloride (CPC), and (ii) one or more flavoring oils which are substantially insoluble in water at room temperature, wherein the ratio of the CPC to the one or more flavoring oils is from 1:1.5 to 1:2.5.

2. The liquid oral care composition of claim 1 wherein the ratio of the CPC to the one or more flavoring oils is 1:1.6 to 1:1.9.

3. The liquid oral care composition of claim 1 or claim 2 wherein the CPC and the one or more flavoring oils form a micelle or a water-in-oil microemulsion in aqueous media at room temperature.

4. The liquid oral care composition of any of the foregoing claims wherein the one or more flavoring oils comprise menthol.

5. The liquid oral care composition of any of the foregoing claims wherein the one or more flavoring oils comprise menthol, spearmint oil, peppermint oil, or combinations of any of these.

6. The liquid oral care composition of any of the foregoing claims wherein the one or more flavoring oils comprise a combination of menthol, spearmint oil and peppermint oil in a ratio to CPC as follows:

   1 part CPC :

   0.3 – 0.9 parts menthol :

   0.4 – 1.2 parts spearmint oil :

   0.1 – 0.5 parts peppermint oil.

7. The liquid oral care composition of any of the foregoing claims wherein the one or more flavoring oils comprise a flavoring component comprising

   i) menthol, e.g. in an amount of at least 15%, e.g., 15-25%, e.g. about 20% by weight of flavoring component;

ii) peppermint oil (e.g., natural peppermint oil, synthetic peppermint oil, cornmint oil or mixtures thereof), e.g., in an amount of at least 10%, e.g., 10-20%, e.g., about 15% by weight of flavoring component;

iii) spearmint oil, e.g., in an amount of 30-55%, e.g., 40-50%, about 45% by weight of flavoring component;

wherein the composition may optionally comprise coolants and/or sweeteners in addition to the flavor component.

8. The liquid oral care composition of any of the foregoing claims in the form of a mouthrinse.

9. The liquid oral care composition of any of the foregoing claims comprising 0.05-0.07% total menthol.

10. The liquid oral care composition of any of the foregoing claims which is a water-in-oil microemulsion or micellar system.

11. The liquid oral care composition of any of the foregoing claims wherein the one of more flavoring oils are selected from one or more of menthol, spearmint oil, peppermint oil, carvone, methyl salicylate, anethole, thymol, eugenol, coolants, cinnamic aldehydes, and mixtures thereof.

12. The liquid oral care composition of any of the foregoing claims further comprising one or more parabens.

13. The liquid oral care composition of any of the foregoing claims further comprising non-caloric sweeteners selected from saccharin, sugar alcohols, and mixtures thereof.

14. The liquid oral care composition of any of the foregoing claims further comprising humectants, selected from propylene glycol, glycerin or mixtures thereof.

15. The liquid oral care composition of any of the foregoing claims further comprising one or more poloxamers.

16. The liquid oral care composition of any of the foregoing claims further comprising an effective concentration of a fluoride ion source.

17. The liquid oral care composition of claim 1 comprising the following ingredients, by weight:

i)	sorbitol	4-7%,
ii)	glycerin, propylene glycol and combinations thereof	12-18%
iii)	sodium fluoride	0.04 – 0.06%
iv)	cetylpyridinium chloride	0.05 – 0.1%
v)	sodium saccharin	0.01- 0.03%
vi)	polaxamer 407	0.3 - 0.5%
vii)	flavoring component	0.1 – 0.3%
viii)	menthol / coolant (in addition to flavoring component)	0.02-0.06%
ix)	dye	0.0 – 0.01%
x)	parabens	0.02 – 0.06%
xi)	water	75 - 85%

wherein the flavoring component (vii) comprises 85-100% insoluble flavoring oils.

18. A method of prophylaxis and/or treatment of a disease or condition selected from one or more of dry mouth, halitosis, gingivitis, tooth decay, and cavities, comprising administering an effective amount of a liquid oral care composition according to any of the foregoing claims to a subject in need thereof.

19. Use of cetyl pyridinium chloride (CPC) together with one or more flavoring oils which are substantially insoluble in water at room temperature, in a ratio of the CPC to the one or more flavoring oils from 1:1.5 to 1:2.5, in the manufacture of a liquid oral care composition, e.g. according to any of the foregoing claims, for prophylaxis and/or treatment of a disease or condition selected from one or more of dry mouth, halitosis, gingivitis, tooth decay, and cavities.

20. A method of making a liquid oral care composition according to any of claims 1-17 comprising adding flavoring oils to an aqueous solution comprising cetylpyridinium chloride and mixing until the composition is clear.

21. The method of claim 20 comprising adding colorant to water and mixing, then adding sodium saccharide, sodium fluoride and CPC and mixing, then adding a poloxamer and mixing, then adding add sorbitol and glycerin and mixing, and then adding a mixture of propylene glycol, parabens, and menthol and optionally other flavorings, and mixing until the composition is clear.