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Anti-calculus oral hygiene compositions

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Anticalculus Oral Hygiene Compositions

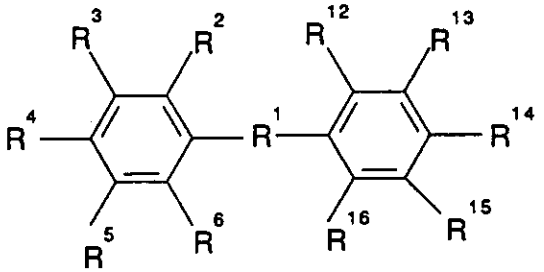
The present invention relates to oral hygiene compositions, in particular compositions comprising a tripolyphosphate salt and a non-cationic anti-bacterial agent, which compositions are useful in the inhibition of dental calculus and plaque.

GB 2 200 551-A and GB 2 230 188-A (to Colgate-Palmolive) disclose compositions having anti-calculus and anti-plaque activity, the former being provided by a linear molecularly dehydrated polyphosphate salt which is preferably a pyrophosphate salt, and the latter being provided by a non-cationic anti-bacterial agent such as a hydroxydiphenylether, preferably triclosan. The preferred pH for such compositions is in the range 5.5 to 8. No examples comprising a tripolyphosphate are provided.

This application is a divisional application, the parent application being No. 9010258.3 (GB 2 232 591-A).

It has now been found that a useful oral hygiene composition may be provided having, in addition to anti-calculus activity, anti-plaque activity, by combining a tripolyphosphate salt and an anti-bacterial compound.

Accordingly, the present invention provides an oral hygiene composition which comprises: an anti-calculus agent comprising a water-soluble alkali metal tripolyphosphate saltpresent in at least 4% by weight of the composition; a substantially water insoluble noncationic anti-bacterial agent ~~which is a diphenyl ether~~ of the formula (I):



(I)

in which R^1 is oxygen, sulphur, or an alkylene group of from one to six carbon atoms and each of R^2 to R^6 and R^{12} to R^{16} is hydrogen, hydroxyl or a halogen; and an orally acceptable vehicle; the pH of which composition is from 8 to 10.

Examples of compounds of formula (I) include, for example,
5, 5'-dichloro-2, 2'-dihydroxydiphenylmethane;

2, 2'-dihydroxy-3, 5, 6, 3', 5', 6'-hexachlorodiphenylmethane;
3, 3'-dibromo-5, 5'-dichloro-2,2'- dihydroxydiphenylether and
2, 4, 4'-trichloro-2'-hydroxydiphenyl ether (triclosan); of which triclosan is particularly preferred.

The noncationic anti-bacterial agent is preferably present in from 0.01 to 2.0%, more preferably 0.05 to 1.0% by weight of the composition.

The oral hygiene composition may be presented in any of the conventional formulations such as a dentifrice, including toothpaste, a mouthwash or a formulation that is chewed or sucked by the user such as a lozenge or a chewing gum. Suitably the oral hygiene composition is in the form of a toothpaste composition which comprises an abrasive.

It will be appreciated that the alkali metal tripolyphosphate salt is included in compositions of the invention as an anti-calculus agent. In some instances, the anti-calculus agent may consist essentially of the water-soluble alkali metal tripolyphosphate salt.

Suitable water-soluble alkali metal salts include sodium or potassium tripolyphosphate which may be used in the hydrated or unhydrated forms. Preferably the tripolyphosphate salt is present in from about 4 to about 6% by weight, based on the total weight of the composition.

Preferably the pH of the composition is from about 8 to about 9. When the composition comprises a compound of formula (I), a pH of above 8 is found to enhance the availability of the compound of formula (I). All references to the pH of the composition herein are references to the pH of the composition measured without dilution of the composition.

Suitable abrasives for use in the present invention include silica, plastics particles, alumina, calciuim carbonate, zinc orthophosphate and calcium pyrophosphate. Silica is especially preferred.

Silica abrasives are well known and commercially available, generally having an

average particle size ranging between about 0.1 to about 30 microns, such as from about 5 to about 15 microns. Silica dental abrasives useful in the present invention include those marketed by the J.M. Huber Corporation under the trade name 'Zeodent' and the silica zerogels marketed by the W.R. Grace and Company, Davison Chemical Division under the trade name 'Syloid'. US 3 358 230 and US 3 862 307 describe silica dental abrasives that are useful in the toothpaste compositions according to the present invention. The silica abrasive may also be a naturally occurring amorphous silica such as diatomaceous earth. Suitable forms of diatomaceous earth are those marketed under the trade mark 'Celite' by Johns - Manville Products Corporation, for instance 'Celite Superfine Superfloss'.

Plastics dental abrasives are well known and are described in, for example, GB 939 230, GB 995 351 and GB 1 055 784, and US 3 151 027.

Alumina abrasives are well known and commercially available. Preferably the alumina abrasive may be treated with a solution of a surface-treating agent which may be an alkali metal silicate, hydrogen peroxide, an acid or an organophosphorus compound, of which an alkali metal silicate is especially preferred, as described in US 4 781 982 (to Aluminium Company of America).

A calcium carbonate abrasive is preferably used in conjunction with an ionic agent to suppress the formation of free calcium ions, such as an alkali metal carbonate or bicarbonate, or mixture thereof, as described in EP 0 092 929 (to Beecham Group p.l.c.).

Generally, an amount of the dental abrasive suitable for use in the toothpaste composition of the present invention will be empirically determined to provide an acceptable level of cleaning and polishing, in accordance with the techniques well known in the art. Suitably, the abrasive will be present in from about 5 to about 60%, preferably from about 5 to about 30%, by weight of the toothpaste.

Advantageously, compositions of the present invention may further comprise a phosphatase enzyme inhibitor comprising a fluoride ion source, to optimise the anti-calculus activity of the compositions by inhibiting the enzymatic hydrolysis of the tripolyphosphate salt by salivary phosphatase enzymes. The fluoride ion source may be provided by an alkali metal fluoride, preferably sodium fluoride, an alkali metal monofluorophosphate, stannous fluoride and the like. Preferably, however, the fluoride ion source is an alkali metal fluoride, most preferably sodium fluoride, since

this appears to provide enhanced storage stability as compared to other fluoride ion sources. The fluoride ion source serves as a phosphatase enzyme inhibitor, and in addition, the fluoride ion source may also provide an anti-caries effect. Preferably, the fluoride ion source will be used in an amount to provide an anti-caries effective amount and a phosphatase enzyme inhibiting amount, such as an amount sufficient to provide from about 25 ppm to about 3500 ppm, preferably about 1100 ppm, fluoride. It will be appreciated that the fluoride ion source may be included in compositions of the invention to provide a phosphatase enzyme inhibitor. In some instances, the phosphatase enzyme inhibitor may consist essentially of a fluoride ion source.

Suitably, in compositions of the present invention, the orally acceptable vehicle may comprise a thickening agent, a binding agent and a humectant. Preferred thickening and binding agents include for example natural and synthetic gums such as xanthan gums, carageens, alginates, cellulose ethers and esters and silica. When the abrasive is silica, it is preferred to use a thickening silica as the thickening agent. Preferred humectants include glycerin, sorbitol, propylene glycol and polyethylene glycol. A preferred humectant system consists of glycerin, sorbitol and polyethylene glycol.

In addition, the orally acceptable vehicle may optionally comprise surfactants, sweetening agents, flavouring agents, anticaries agents (in addition to the fluoride ion source provided as a phosphatase enzyme inhibitor), anti-bacterial agents such as cetyl pyridinium chloride, tooth desensitizing agents, colouring agents and pigments. Useful surfactants include the water-soluble salts of alkyl sulphates having from 10 to 18 carbon atoms in the alkyl moiety, such as sodium lauryl sulphate, but other anionic surfactants as well as non-ionic, zwitter-ionic, cationic and amphoteric surfactants may also be used.

When the preferred aqueous orally acceptable dental vehicle is employed, a toothpaste composition of the present invention suitably contains from about 10 to about 80% humectant, from about 0.25 to about 5% detergent, from 0 to about 2% sweeteners and flavouring agents together with water and an effective amount of binding and thickening agents, such as from about 0.1% to about 12%, to provide the toothpaste of the invention with the desired stability and flow characteristics.

Toothpaste compositions according to the present invention may be prepared by admixing according to conventional practice the tripolyphosphate salt, the dental abrasive and, if included, the fluoride ion source with the orally acceptable dental vehicle, which may be anhydrous but is preferably an aqueous orally acceptable

dental vehicle, to form a storage stable semi-solid extrudable material useful as a toothpaste The pH thereof may be adjusted if necessary and desired, by the addition of, for instance sodium hydroxide. Preferably, the tripolyphosphate salt is in powder form when incorporated into the vehicle, as this tends to enhance the stability of the resulting toothpaste.

Toothpaste compositions of the present invention may also be prepared in the form of a paste of a uniform colour or in the form of a striped toothpaste. A suitable aparatus for filling toothpaste tubes with striped toothpaste is described in GB 962 757. In accordance with this patent, toothpastes of different colours are fed through separate tubes of a bundle of tubes that is inserted into a toothpaste container and gradually moved relative to the container as the container is filled.

In a preferred aspect, the present invention provides a toothpaste composition comprising an anticalculus agent comprising a water-soluble alkali metal tripolyphosphate salt present in at least 4% by weight of the composition; a substantially water insoluble noncationic anti-bacterial agent of formula (I) as hereinbefore defined; a silica abrasive and an orally acceptable vehicle; the toothpaste having a pH of from about 8 to about 10.

In a further aspect, the present invention provides a composition as hereinbefore defined for use in oral hygiene.

The invention will now be illustrated by the following examples:

Examples 1 - 4 - Striped dentifrices

The preparation of striped dentrifrices is well known in the art. US Patent Nos. 3 996 863, 3 980 767, 4 328 205 and 4 358 437 described toothpastes and methods for production thereof which may be utilised for the production of the dentifrices according to the present invention.

Example 1

A striped dentifrice according to the present invention and comprising a central core with red stripes and aqua stripes was prepared by combining the ingredients set forth below according to known conventional techniques.

		%w/w		
		Core	Red	Aqua
PEG* 400		3.00	3.00	3.00
Xanthan Gum		0.70	0.70	0.70
Sodium Fluoride		0.24	0.24	0.24
Sodium Saccharin		0.21	0.21	0.21
Triclosan		0.20	0.20	0.20
Sorbitol (70%)		29.09	29.09	29.09
FD + C Blue No.1 dye		-	-	0.0020
D + C Yellow No. 10 dye		-	-	0.0002
Titanium Dioxide		1.459	-	-
Abrasive Silica		14.00	14.00	14.00
Thickening Silica		8.00	8.00	8.00
Sodium Tripolyphosphate		5.00	5.00	5.00
Glycerine		10.00	10.00	10.00
NaOH		0.45	0.45	0.45
Flavour		0.80	0.80	0.80
Sodium Lauryl Sulphate		1.15	1.15	1.15
Deionized Water	to	100.00	100.00	100.00

*PEG denotes polyethylene glycol.

Example 2

As Example 1 but with triclosan at 0.3%.

Example 3

		% w/w		
		Core	Red	Aqua
PEG* 300		3.00	3.00	3.00
Xanthan Gum		0.60	0.60	0.60
Sodium Fluoride		0.22	0.22	0.22
Sodium Saccharin		0.20	0.20	0.20
Triclosan		0.20	0.20	0.20
Sorbitol (70%)		27.70	27.70	27.70
FD + C Blue No.1 dye		-	-	0.002
D + C Yellow No. 10 dye		-	-	0.001
D + C Yellow No. 3 dye		-	0.10	-
Titanium Dioxide		1.45	-	-
Abrasive Silica		14.00	14.00	14.00
Thickening Silica		7.00	7.00	7.00
Sodium Tripolyphosphate		5.00	5.00	5.00
Glycerine		20.00	20.00	20.00
Flavour		0.80	0.80	0.80
Sodium Lauryl Sulphate		1.70	1.70	1.70
Deionized Water	to	100.00	100.00	100.00

*PEG denotes polyethylene glycol.

Example 4

As Example 4 but with triclosan at 0.3%.

Reference Example 1

Toothpastes A (as per example below), B, C, and D were prepared using a silica dental abrasive, sodium tripolyphosphate (STP), and sodium fluoride in an amount to provide 1100 ppm fluoride, in an aqueous orally acceptable vehicle. The amounts of STP and the pH of the toothpastes were varied as shown in the Table below:

Table

Tooth-paste	pH*	STP %	% STP As % Of Initial STP After			
			1 year	2 year	3 year	5 year
A	9	4.3	98	96	94	91
B	7	4.3	96	93	89	85
C	9	3.0	90	80	69	59
D	7	2.8	85	70	55	39

*The pH's reported are nominal values.

The data presented in the Table were derived from storage stability tests on actual samples of the four toothpastes, with the storage stabilty data regressed to provide predicted stability over four years of storage at room temperature with a confidence level of 95%.

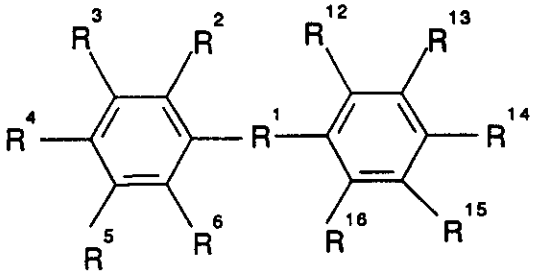
Toothpaste		**% w/w**
Polyethylene glycol (PEG-8)		3.00
Xanthan Gum		0.70
D + C Red No. 30 Lake		0.02
FD + C Blue No. 1 (0.2%)		0.17
D + C Yellow No. 10 (0.20%)		0.24
Sodium Fluoride		0.24
Sorbitol (70%)		29.61
Sodium Saccharin		0.21
Thickening Silica		8.00
Abrasive Silica		14.00
Titanium Dioxide		0.96
Glycerine 99%		10.00
Sodium Tripolyphosphate (Food Grade)*		5.00
Sodium Hydroxide (25%)		1.80
Flavour		0.80
Sodium Lauryl Sulphate		1.15
Deionized Water	to	100.00

* Food grade has a nominal purity of 92%.

Initial pH 8.4

Claims

1. An oral hygiene composition which comprises:
an anti-calculus agent which is a water-soluble alkali metal tripolyphosphate salt present in at least 4% by weight of the composition; a substantially water insoluble noncationic anti-bacterial agent ~~which is a diphenylether~~ of the formula (I):



(I)

in which R^1 is oxygen, sulphur, or an alkylene group of from one to six carbon atoms and each of R^2 to R^6 and R^{12} to R^{16} is hydrogen, hydroxyl or a halogen; and an orally acceptable vehicle; the pH of which composition is from 8 to 10.

2. A composition as claimed in claim 1 in which the noncationic anti-bacterial agent is present in from 0.01 to 2.0% by weight of the composition.

3. A composition as claimed in claim 2 in which the noncationic anti-bacterial agent is present in from 0.05 to 1.0% by weight of the composition.

4. A composition as claimed in claims any one of 1 to 3 in which the compound of formula (I) is selected from the group consisting of
5, 5'-dichloro-2, 2'-dihydroxydiphenylmethane;
2, 2'-dihydroxy-3, 5, 6, 3', 5', 6'-hexachlorodiphenylmethane;
3, 3'-dibromo-5,5'-dichloro-2,2'- dihydroxydiphenylether; and
2, 4, 4'-trichloro-2'- hydroxydiphenylether.

5. A composition as claimed in any one of claims 1 to 4 which is in the form of a toothpaste and comprises an abrasive.

6. A composition as claimed in claim 5 in which the abrasive is selected from silica, plastics particles, alumina, calcium carbonate, zinc orthophosphate or calciium pyrophosphate.

7. A composition as claimed in claim 5 or 6 in which the abrasive is present in

from 5 to 60% by weight of the toothpaste.

8. A composition as claimed in claim 6 or 7 in which the abrasive is silica and the orally acceptable vehicle comprises a thickening silica.

9. A composition as claimed in any one of claims 1 to 8 in which the anti-calculus agent consists essentailly of the water-soluble alkali metal tripolyphosphate salt.

10. A composition as claimed in any one of claims 1 to 9 in which the alkali metal tripolyphosphate salt is sodium or potassium tripolyphosphate.

11. A composition as claimed in any one of claims 1 to 10 in which the alkali metal tripolyphosphate salt is present in from 4 to 6% by weight of the composition.

12. A composition as claimed in any one of claims 1 to 11 in which the pH of the composition is from 8 to 9.

13. A composition as claimed in any one of claims 1 to 12 further having a phosphatase enzyme inhibitor comprising a fluoride ion source.

14. A composition as claimed in claim 13 in which the a phosphatase enzyme inhibitor consists essentailly of a fluoride ion source.

15. A composition as claimed in claim 13 or claim 14 in which the fluoride ion source is an alkali metal fluoride.

16. A composition as claimed in claim 15 in which the alkali metal fluoride is sodium fluoride.

17. A composition as claimed in any one of claims 13 to 16 in which fluoride ion source provides from about 25 ppm to about 3500 ppm of fluoride.

18. A composition as claimed in any one of the preceding claims in which the orally acceptable vehicle comprises a humectant system which consists of glycerin, sorbitol and polyethylene glycol.

19. An toothpaste composition comprising an anticalculus agent comprising a

water-soluble alkali metal tripolyphosphate salt present in at least 4% by weight of the composition; a substantially water insoluble noncationic anti-bacterial agent of formula (I), as defined in claim 1; a silica abrasive and an orally acceptable vehicle; the toothpaste having a pH of from 8 to 10.

20. A composition as defined in any one of the preceding claims in the form of a striped toothpaste.

21. A composition as defined in any one of the preceding claims for use in therapy.

22. The use of a water-soluble alkali metal tripolyphosphate salt and a substantially water insoluble noncationic anti-baterial agent of formula (I), as defined in claim 1, in the manufacture of an oral hygiene composition for inhibiting dental caculus and dental plaque.

23. A process for the preparation of a composition as defined in any one of claims 1 to 22 which process comprises admixing the ingredients in the appropriate quantities and if necessary or desired, adjusting the pH.

24. A composition substantially as hereinbefore described with reference to any one of Examples 1 to 4.

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Title NOVEL COMPOSITIONS

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