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(19)

(54) ORAL HYGIENE COMPOSITIONS

(71) We, BEECHAM GROUP LIMITED, a British Company, of Beecham House, Great West Road, Brentford, Middlesex, England, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to oral hygiene compositions having anti-cariogenic activity.

In the past few years many proposals have been made to incorporate various fluoride compounds into oral hygiene compositions such as dentifrices in order to provide them with anti-cariogenic activity. A particular fluoride that has found favour for this purpose is sodium monofluorophosphate, though the use of other water-soluble monofluorophosphates has also been proposed. An important effect of these monofluorophosphates is the fact that the solubility of tooth enamel in weakly acid media is reduced.

We have now also found that the activity of monofluorophosphates in reducing the solubility of tooth enamel is enhanced when these are used in admixture with certain proportions of calcium glycerophosphate or calcium phytate. These results are surprising because we have shown, for example, that there is no potentiation when sodium glycerophosphate or sodium phytate is employed in conjunction with sodium monofluorophosphate. Moreover, we have also shown that there is no potentiation of the solubility-reducing properties of monofluorophosphate when this is used in conjunction with inorganic calcium salts such as calcium chloride.

Accordingly, the present invention provides oral hygiene compositions comprising a monofluoro phosphate salt in an amount to provide 0.01 to 1% of fluorine based on the weight of the composition and calcium glycerophosphate or calcium phytate in an amount to provide a weight ratio of monofluorophosphate to phytate or glycerophosphate of 10:1 to 1:1.

The water-soluble monofluorophosphate is preferably sodium monofluorophosphate. This compound may contain impurities such as sodium fluoride or water-soluble sodium phosphate. These are not deleterious, but the sodium monofluorophosphate material employed should have a total fluoride content of above 12%, preferably above 12.7%; a content of not more than 1.5%, preferably not more than 1.2%, of free sodium fluoride; and a sodium monofluorophosphate content of at least 12%, preferably at least 12.1%, all calculated as fluorine. Alternative potassium, ammonium, lithium, calcium, magnesium, zinc or stannous monofluorophosphates of comparable purity can be employed alone or in admixture with each other or with sodium monofluorophosphate. Also the term "monofluorophosphate" as used herein includes monofluoropolyphosphates, such as those of the formula:

$Na_4P_3O_9F$; $K_4P_3O_9F$; $(NH_4)_4P_3O_9F$; $Na_3KP_3O_9F$; $(NH_4)_3NaP_3O_9F$ and $Li_4P_3O_9F$.

The amount of monofluorophosphate used is dependent to some extent on the type of monofluorophosphate, its solubility and the type of dentifrice composition, and should be an effective, but non-toxic, amount. The monofluorophosphate is present in the oral hygiene composition in an amount to provide 0.01% to 1% of fluorine based on the weight of the composition. Thus, sodium monofluorophosphate is employed in an amount of 0.08 to 7.6% by weight of the composition.

The inclusion of calcium glycerophosphate

in dentifrices is disclosed in British Patent Specification No. 572,352, but with no reference to the concomitant presence of a monofluorophosphate and no reference to the ratios now identified. Accordingly, the aforesaid potentiation of the monofluorophosphate by calcium glycerophosphate has not hitherto been appreciated.

The calcium glycerophosphate or calcium phytate is present in the compositions of the invention in an amount such that the weight ratio of monofluorophosphate to the total calcium glycerophosphate or calcium phytate present is within the range of 10:1 to 1:1, preferably 10:1 to 3:1. The preferred embodiment of the invention utilises sodium monofluorophosphate and calcium phyate or glycerophosphate in a molar ratio of about 8:1 (i.e. a weight ratio of about 5:1 for calcium glycerophosphate and about 1.1:1 for calcium phytate).

The oral hygiene compositions of the invention are often in the form of dentifrices and these will also usually contain polishing agents, surfactants, gelling agents and other excipients such as flavouring and colouring agents. The compositions may be in the form of powders, pastes or liquids. A particularly useful form of composition is one in the form of a gel.

The polishing agent may be selected from those currently employed for this effect, in dental preparations. For instance there may be employed water-insoluble sodium or potassium metaphosphate, hydrated or anhydrous dicalcium phosphate, calcium pyrophosphate, zirconium silicate or mixtures thereof. Particularly useful polishing agents are various forms of silica, especially silica xerogels as described in U.S. Patent No. 3,538,230. The polishing agent is generally finely-divided with a particle size smaller than 10 microns, preferably of between 2 and 6 microns. The polishing agent may be employed in an amount of from 10 to 99% by weight of the dentifrice. Preferably the dentifrice compositions are in the form of pastes containing 20 to 75% of the polishing agent, though these can be in the form of powders containing 70 to 99% of the polishing agent.

A suitable surfactant is normally included in the dentifrice compositions, preferably this being a water-soluble non-soap synthetic organic detergent. Suitable detergents are the water-soluble salts of: higher fatty acid monoglyceride monosulphates (for example sodium hydrogenated coconut fatty acid monoglyceride monosulphate); higher alkyl sulphates (for example sodium lauryl sulphate); alkylarylsulphonates (for example sodium dodecylbenzene-sulphonates); and higher alkyl sulphoacetates (for example sodium lauryl sulphoacetate). There may also be used the saturated higher aliphatic acyl amides of lower aliphatic amino carboxylic acids having 12 to 16 carbon atoms in the acyl radical and in which the amino acid portion is derived from the lower aliphatic saturated monoaminocarboxylic acids having 2 to 6 carbon atoms, such as the fatty acid amides of glycine, sarcosine, alanine, 3-aminopropanoic acid and valine, particularly the N-lauryl, myristoyl and palmitoyl sarcosinate compounds. Conventional non-ionic surfactants may also be included if desired.

The surface-active materials are generally present in an amount of 0.05 to 10%, preferably 0.5 to 5% by weight of the dentifrice composition.

The tooth powders and pastes are prepared in the usual manner. Thus the constituents can be mixed in the dry state or as slurries or solutions. It is often advantageous to employ the organic phosphate in the form of an aqueous solution.

In general the liquids in the dental cream or paste will comprise chiefly water, glycerol, sorbitol or propylene glycol, including suitable mixtures thereof. It is advantageous usually to use a mixture of water and glycerol, preferably in combination with sorbitol. A gelling agent such as the natural and synthetic gums and gum-like materials, preferably Irish Moss or sodium carboxymethylcellulose, may be used. Other gums which may be used are gum tragacanth, polyvinyl-pyrrolidone and starch. They are usually used in an amount up to 10%, preferably 0.5 to 5% by weight of the toothpaste.

The pH of the dental cream or an aqueous slurry of the tooth powder is substantially neutral such as a pH of about 6 to 8. If desired, a small amount of acid such as citric acid or an alkaline material may be added.

Other materials may be added such as soluble saccharin, flavouring oils (e.g. oils of spearmint, peppermint, wintergreen), colouring or whitening agents (e.g. titanium dioxide), preservative (e.g. sodium benzoate), emulsifying agents, acidifying agents (e.g. citric acid), silicones, alcohol, menthol and chlorophyll compounds (e.g. sodium copper chlorophyllin).

The compositions of the invention may also be in the form of other oral hygiene compositions, for example, the essential monofluorophosphate and polyol phosphate ingredients may be incorporated in mouth washes, which can be of the suspension type, or in compositions which will be chewed by the user, for example, chewing gum, tablets, pastilles and lozenges. These compositions will contain the conventional base materials together with suitable flavours and sweetening agents.

The compositions of the invention are illustrated by the following Examples in which quantities are expressed on a weight basis.

Examples 1–4	Example			
Ingredient	1	2	3	4
Chalk	49.0	49.0	47.9	47.9
Sorbitol (70% solution)	13.0	13.0	–	–
Glycerol	13.0	13.0	26.0	26.0
Magnesium aluminium silicate	0.75	0.75	0.75	0.75
Calcium silicate	–	–	0.2	0.2
Sodium carboxymethyl cellulose	1.0	1.0	0.9	0.9
Sodium lauryl sulphate	1.5	1.5	1.15	1.15
Sodium monofluorophosphate	0.8	0.8	0.8	0.8
Calcium phytate	0.5	0.1	0.1	–
Calcium glycerophosphate	–	–	–	0.2
Saccharin	0.2	0.2	0.1	0.1
Anticorrosive	0.5	0.5	–	–
Flavour	q.s.	q.s.	q.s.	q.s.
Water	to 100%	to 100%	to 100%	to 100%

The efficacy of these formulations is shown, for example, by tests carried out on the composition of Example 3. Discs of hydroxyapatite were prepared by blending it with 7.5% of polyethylene to improve binding characteristics followed by moulding separate discs by compression at 5000 kg. for one minute and subsequent heating to 160°C. Separate discs were treated with a slurry of the dentifrice of Example 3 with water (water:dentifrice = 2:1) using a brushing apparatus for one minute. Some of the discs were then stored for two days in a humid atmosphere. Comparative discs were treated in which the dentifrice composition omitted the calcium phytate. The treated discs were each placed beneath a rotating propeller in acetic acid buffer at pH 4.65 and 37°C for one hour. The percentage solubility reduction relative to treatment with an identical dentifrice but containing no fluorophosphate or organic phosphate was determined in each case as with the preceding experiments. The results are set out in Table I.

TABLE I

Composition	Solubility Reduction Achieved	
	Immediate Dissolution	Dissolution after storage
Example 3	8.5%	12.5%
Comparative Example without calcium phytate	3.5%	9.0%

Similar experiments were carried out using the compositions of Examples 3 and 4, but the discs were compressed at 10,000 kg. and 110°C and treated with a slurry of concentration, water:dentifrice = 1:1 for two minutes. Only immediate dissolution tests were performed. The results are given in Table II.

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TABLE II

Composition	No. of tests	Solubility Reduction Achieved
Example 3	3	32%
Example 4	3	26%
Comparative Example without organic Phosphate	3	13%

Example 5

Ingredient	5
Chalk	49.0
Sorbitol (70% solution)	13.0
Glycerol	13.0
Magnesium aluminium silicate	0.75
Sodium carboxymethyl cellulose	1.0
Sodium lauryl sulphate	1.5
Sodium monofluorophosphate	0.8
Calcium glycerophosphate	0.2
Saccharin	0.2
Anticorrosive	0.5
Flavour	q.s.
Water	to 100%

Examples 6–8	Example		
Ingredient	6	7	8
Chalk	–	11.0	6.5
Dicalcium phosphate dihydrate	–	–	4.0
Silica xerogel (Syloid 74)	14.0	–	–
Silica aerogel (Syloid 244)	6.0	11.0	7.0
Pyrogenic silica (Aerosil 200)	–	–	2.5
Glycerol	30.0	50.0	50.0
Sorbitol (70% solution)	43.0	14.0	14.0
Sodium carboxymethyl cellulose	0.8	0.8	0.55
Sodium lauryl sulphate	1.5	1.5	1.5
Sodium monofluorophosphate	0.8	0.8	0.8
Calcium glycerophosphate	0.2	–	0.2
Calcium phytate	–	0.2	–
Saccharin	q.s.	q.s.	q.s.
Flavour	q.s.	q.s.	q.s.
Dye	q.s.	q.s.	q.s.
Water	to 100%	to 100%	to 100%

Syloid and Aerosil are Registered Trade Marks.

Examples 9—10

Compositions 9 and 10 were prepared respectively as for Example 7 but with the amount of calcium phytate being reduced to 0.1% (Example 9) and with the calcium phytate being replaced by 0.2% calcium glycerophosphate (Example 10). Tests were performed as for Table II with 1 and 2 minutes of application of the dentifrice slurry to the disc. The results obtained are given in Table III wherein the comparative composition omitted entirely the organic phosphate.

TABLE III

Composition	Time of Application (mins.)	Solubility Reduction Achieved
9	2	26%
10	2	27.4%
Comparative	2	13%
10	1	10%
Comparative	1	3%

WHAT WE CLAIM IS:—

1. Oral hygiene compositions comprising a monofluorophosphate salt in an amount to provide 0.01 to 1% of fluorine based on the weight of the composition and calcium glycerophosphate or calcium phytate in an

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Chalk	–	11.0	6.5
Dicalcium phosphate dihydrate	–	–	4.0
Silica xerogel (Syloid 74)	14.0	–	–
Silica aerogel (Syloid 244)	6.0	11.0	7.0
Pyrogenic silica (Aerosil 200)	–	–	2.5
Glycerol	30.0	50.0	50.0
Sorbitol (70% solution)	43.0	14.0	14.0
Sodium carboxymethyl cellulose	0.8	0.8	0.55
Sodium lauryl sulphate	1.5	1.5	1.5
Sodium monofluorophosphate	0.8	0.8	0.8
Calcium glycerophosphate	0.2	–	0.2
Calcium phytate	–	0.2	–
Saccharin	q.s.	q.s.	q.s.
Flavour	q.s.	q.s.	q.s.
Dye	q.s.	q.s.	q.s.
Water	to 100%	to 100%	to 100%

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1. Oral hygiene compositions comprising a monofluorophosphate salt in an amount to provide 0.01 to 1% of fluorine based on the weight of the composition and calcium glycerophosphate or calcium phytate in an

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amount to provide a weight ratio of monofluorophosphate to phosphate ester salt of 10:1 to 1:1.

2. Compositions according to claim 1 wherein the monofluorophosphate is sodium monofluorophosphate.

3. Compositions according to claim 1 or claim 2 wherein the weight ratio of monofluorophosphate to calcium glycerophosphate is within the range 10:1 to 3:1.

4. Compositions according to claim 3 wherein sodium monofluorophosphate and calcium phytate or glycerophosphate are present in a molar ratio of about 8:1.

5. Compositions according to any of the preceding claims in the form of a dentifrice paste conaining 0.05 to 10% by weight of a water-soluble non-soap detergent.

6. Compositions according to claim 5 wherein at least part of the dentifrice is in the form of a clear gel.

7. Oral hygiene compositions substantially as described with reference to any of the aforesaid Examples.

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