70545/87

COMMONWEALTH of AUSTRALIA

PATENTS ACT 1952

APPLICATION FOR A STANDARD PATENT

~~I~~ We BEECHAM GROUP plc.,
of Beecham House,
Great West Road,
Brentford, Middlesex TW8 9BD,
UNITED KINGDOM

LODGED AT SUB-OFFICE
23 MAR 1987
Melbourne

hereby apply for the grant of a Standard Patent for an invention entitled:

'ORAL HYGIENE COMPOSITIONS'

which is described in the accompanying ~~provisional~~ complete specification.

Details of basic application(s):—

Number	Convention Country	Date
8607333	UNITED KINGDOM	25th March, 1986

APPLICATION ACCEPTED AND AMENDMENTS ALLOWED 17-1-90

The address for service is care of DAVIES & COLLISON, Patent Attorneys, of 1 Little Collins Street, Melbourne, in the State of Victoria, Commonwealth of Australia.

Dated this 23rd day of March 1987

To: THE COMMISSIONER OF PATENTS

K. M. Rimington
.....
(a member of the firm of DAVIES & COLLISON for and on behalf of the Applicant).

Davies & Collison, Melbourne and Canberra.

AU/1

COMMONWEALTH OF AUSTRALIA
PATENTS ACT 1952
DECLARATION IN SUPPORT OF CONVENTION
APPLICATION FOR A PATENT

In support of the Application made for a patent for an invention entitled:
ORAL HYGIENE COMPOSITIONS

I, David Roberts of Beecham Pharmaceuticals, Great Burgh, Yew Tree Bottom Road, Epsom, Surrey, KT18 5XQ, England,
do solemnly and sincerely declare as follows:-

1. I am authorised by Beecham Group p.l.c. the applicant for the patent to make this declaration on its behalf.

2. Steven Poile
Karen Molyneux

Of Post Office address:
Beecham Products Research Department, St. George's Avenue, Weybridge, Surrey KT13 ODE, England

~~A~~/All British Subject(s)

~~is~~/are the actual inventor(s) of the invention and the facts upon which the applicant is entitled to make the application are as follows:-

by virtue of the employment of the actual inventor(s) by Beecham Group p.l.c., the applicant would, if a patent were granted upon an application made by the said actual inventor(s), be entitled to have the patent assigned to it.

3. The basic application~~(s)~~ as defined by Section 141 of the Act was/~~were~~ made in United Kingdom by Beecham Group p.l.c. as follows:
Great Britain Patent Appln. No. 8607333 filed on 25th March 1986

4. The basic application~~(s)~~ referred to in the paragraph 3 of this Declaration was/~~were~~ the first application~~(s)~~ made in a Convention country in respect of the invention the subject of the application.

Declared at Epsom, Surrey, England

this 2nd day of March 1987

David Roberts, as Attorney for and on behalf of the said Beecham Group p.l.c.

Witness:

(12) PATENT ABRIDGMENT (11) Document No. AU-B-70545/87
(19) AUSTRALIAN PATENT OFFICE (10) Acceptance No. 595017

(54) Title
ORAL COMPOSITION OF ALKALI/ALKALINE EARTH METAL OXALATE AND A FLUORIDE ION SOURCE

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(71) Applicant(s)
BEECHAM GROUP PLC

(72) Inventor(s)
STEVEN POILE; KAREN MOLYNEUX

(74) Attorney or Agent
DAVIES & COLLISON, MELBOURNE

(56) Prior Art Documents
US 4335102
US 4363794
US 4057621

(57) Claim

1. An anti-caries oral hygiene composition in the form of a dentifrice, mouthwash, tablet, lozenge or pastile comprising:

(i) an anti-caries agent consisting essentially of from greater than 0 to 7% by weight of the composition of alkali metal oxalate or alkaline earth oxalate and from 20 to 1500ppm of fluoride ions;

(ii) a dentally acceptable excipient; and

(iii) a pH of from 4 to 10.

5. A composition according to any one of claims 1 to 4, which is in the form of a dentifrice.

6. A composition according to any one of claims 1 to 4 which is in the form of a mouthwash.

C O M M O N W E A L T H O F A U S T R A L I A

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COMPLETE SPECIFICATION

(Original)

FOR OFFICE USE

Class Int. Class

Application Number: 70545/87
Lodged:

Complete Specification Lodged:
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Priority:

Related Art:

This document contains the amendments made under Section 49 and is correct for printing.

Name of Applicant: BEECHAM GROUP plc

Address of Applicant: Beecham House,
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United Kingdom

Actual Inventor(s): Steven POILE; &
Karen MOLYNEUX

Address for Service: DAVIES & COLLISON, Patent Attorneys,
1 Little Collins Street, Melbourne, 3000.

Complete specification for the invention entitled:

'ORAL HYGIENE COMPOSITIONS'

The following statement is a full description of this invention, including the best method of performing it known to us :-

ORAL HYGIENE COMPOSITIONS

The present invention relates to oral hygiene compositions, and in particular to dentifrices and mouthwashes having improved anticaries effect.

A variety of anticaries agents have hitherto been used in dentifrices and mouthwashes, including alkali metal fluorides and alkali metal monofluorophosphates. It has now been discovered that enhanced anticaries effect can be achieved when a combination of fluoride ions and oxalate ions is used within a specified weight ratio and pH range.

The present invention provides an anti-caries oral hygiene composition in the form of a dentifrice, mouthwash, tablet, lozenge or pastile comprising:

(i) an anti-caries agent consisting essentially of from greater than 0 to 7% by weight of the composition of alkali metal oxalate or alkaline earth oxalate and from 20 to 1500ppm of fluoride ions;

(ii) a dentally acceptable excipient; and

(iii) a pH of from 4 to 10.

The term alkali metal oxalate and/or alkaline earth metal oxalate as used herein includes mixtures of one or more alkali metal oxalates and/or alkaline earth metal oxalates. Suitable oxalates for use in compositions of the invention may include soluble and sparingly soluble oxalates such as sodium, potassium, lithium, calcium, magnesium, barium and strontium. Particularly preferred oxalates are sodium oxalate, potassium oxalate and calcium oxalate or mixtures thereof.

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Preferably the alkali metal oxalate and/or alkaline earth metal oxalate is present in an amount of from 0.0025% to 7% by weight.

The fluoride ions may be provided by an alkali metal fluoride, such as sodium, potassium or lithium fluoride and the use of sodium fluoride is especially preferred. Other suitable fluorides include ammonium, stannous and zinc fluorides.

Alternatively, a monofluorophosphate may be used, preferably an alkali metal monofluorophosphate. Sodium monofluorophosphate, Na_2PO_3F, is especially preferred but the corresponding potassium and/or lithium salts can also be employed. The term 'monofluorophosphate' as used herein includes monofluoropolyphosphates, such as those of formulae $Na_4P_3O_9F$; $K_4P_3O_9F$; $Na_3KP_3O_9F$; $(NH_4)_3NaP_3O_9F$ and $Li_4P_3O_9F$.

If desired, a mixture of ionic fluoride and monofluorophosphate may be employed. The total amount of fluoride and monofluorophosphate used is dependent to some extent on the type of composition, but it should be an effective, but non-toxic, amount. Typically the fluoride(s) is present in the oral hygiene composition in an amount to provide a total of from 0.025 to 0.25% of fluorine based on the weight of the oral hygiene composition. The preferred total fluoride level is from 0.05 to 0.15% by weight of the composition.

Preferably, the composition is in the form of a dentifrice, and in this form will usually include a dentally acceptable abrasive. Suitable abrasives are

insoluble calcium salts such as calcium carbonate, dicalcium phosphate and calcium pyrophosphate; aluminia, silica and synthetic plastic resin particles.

The silica abrasive can be a precipitated silica or a silica gel, such as the silica xerogels described in US Patent No. 3538230. Preferred silica xerogels are marketed under the trade name 'Syloid' by W.R. Grace and Company, Davison Chemical Division. Preferred precipitated silicas are those marketed under the trade name 'Zeodent' by the J.M. Huber Corporation.

The amount of abrasive will be within conventional limits, and will normally vary from 15% to 50% by weight of the composition.

The compositions of the invention may optionally contain other agents known to enhance the anticaries effect of fluoride and monofluorophosphate, such as calcium glycerophosphate, this being incorporated in a weight ratio of up to 1:13, preferably 1:20 to 1:3, to the total weight of fluoride and/or monofluorophosphate salts.

The composition of the invention may be presented in conventional dentifrice dental cream and dental powder formulations, or as a conventional mouthwash formulation.

The compositions of the invention will also usually contain surfactants, gelling agents and other excipients such as flavouring and colouring agents.

The surfactant is normally a water-soluble non-soap or synthetic organic detergent. Suitable sorfactants include 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); alkylarysulphonates (for example sodium dodecylbenzenesulphonates); 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 mono-amino carboxylic 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-lauroyl, 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 15%, preferably 0.5 to 5% by weight of the composition.

The tooth powders and pastes are prepared in the usual manner. Thus, the ingredients can be mixed in the dry state or as slurries or solutions.

In general the liquid in the dental cream or paste will comprise chiefly water, glycerine, sorbitol and/or a glycol, including suitable mixtures thereof. Suitably, the glycol is propylene glycol or a polyethylene glycol. It is preferred to use also a gelling agent in dental creams, such as natural or synthetic gums or gum-like materials, e.g. Irish Moss, gum tragacanth, sodium carboxymethylcellulose, polyvinylpyrrolidone or starch. Irish Moss and sodium carboxymethylcellulose

are preferred gelling agents. The gum content is usually up to 10% and preferably 0.01 to 5% by weight of the preparation.

Other materials may be added, such as sweetening agents, for example soluble saccharine, flavouring oils (e.g. oils of spearmint, wintergreen, peppermint), chloroform, colouring or whitening agents (e.g. titanium dioxide), preservative (e.g. sodium benzoate), emulsifying agents, silicones, alcohol, menthol, chlorophyllin), antibacterial agents (e.g. chlorhexidine), anti-plaque agents, anti-calculus agents, and agents for sensitive dentine (e.g. strontium salts, formaldehyde).

The compositions of the invention may also be in the form of other oral hygiene compositions, for example, the ingredients may be incorporated in mouthwashes 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 and may be formulated in known manner.

Oral hygiene compositions of the present invention have been found to inhibit glucose utilisation and lactate production by common oral microorganisms, and this appears to be the mechanism by which the improved anticaries effect of the compositions is achieved.

The compositions for the invention are illustrated by the following examples:

	Example I % w/w	Example II
Glycerine	24.00	
15% Saccharine solution	2.00	
Guar gum	1.00	as in Ex I
TiO_2	1.00	
NaF	0.22	0.11
NaMFP	-	0.38
Nipagin	0.05	
Nipasol	0.05	
[1]Sipernat 22S (Thickening silica)	6.00	
[2]Tixosil 53 BE (Abrasive Silica)	14.00	as in Ex I
Flavour	1.00	
[3]Adinol C7 (Detergent)	2.00	
Sodium Oxalate	5.00	2.5
Water	to 100%	

	Example III % w/w	Example IV
Glycerine	4.00	10.00
70% sorbitol	16.00	10.00
15% Saccharine solution	2.00	2.00
Na carboxy methyl cellulose	1.50	1.20
Hydroxy ethyl cellulose	0.10	-
Calcium glycerophosphate	0.065	-
Polyvinyl pyrrolidone	0.10	
Na MFP	0.38	0.76
NaF	0.11	0.10
Na_2CO_3	0.50	-
$NaHCO_3$	1.50	-
Sodium lauryl sulphate	1.88	1.60
Hydrated silicone dioxide	4.00	-
Flavour	1.00	1.00
TiO_2	-	-
Sodium oxalate	2.50	3.00
Di calcium phosphate		46.00
Na_2HPO_4		1.00
Water	to 100.00	100.00

[1] Trade mark of Rhone-Poulenc

[2] Trade mark of Degussa

[3] Trade mark of Croda

	EXAMPLE V % w/w
70% sorbitol	30.00
30% saccharin	1.40
Na carboxy methyl cellulose	1.50
Hydroxy ethyl cellulose	0.10
Polyvinyl pyrrolidine	0.10
NaMFP	0.76
CaGP	0.13
Calcium carbonate	35.00
Sodium lauryl culphate	1.88
10.2% NaOH	1.00
calcium oxalate	2.00
Flavour	1.15
Sipernat 22S	2.00
Water	to 100.00

EXAMPLE VI

A plaque pH study was carried out using mouthwash solutions according to the invention. Sixteen subjects were used each of which abstained from dental hygiene for 24 hours prior to the test and did not eat or drink for one hour before the test. Subjects each rinsed for 1 minute with 10ml of each of the 5 products under test.

Thirty minutes later plaque was sampled from the subjects molar and pre-molar teeth. the sample was mixed with 20µl of saline and the pH recorded. The subjects then rinsed for 1 minute with 10ml of a 10% w/v sucrose solution and 10 minutes later a further plaque sample was taken from the posterior teeth. The plaque pH was measured as described earlier.

Each subject used each product in a balanced randomised order, the study being double blind in nature.

Results are indicated below

Test mouthwash	Post challenge Plaque pH ± s.d
25 ppm F	5.68 ± 0.29
25ppmF + 0.025% Na oxalate	5.68 ± 0.25
25 ppm F + 0.05% Na oxalate	5.74 ± 0.32
25 ppm F + 0.10% Na oxalate	5.84 ± 0.31
0.05% Na oxalate	5.69 ± 0.24

The post challenge pH after rinsing with 25 ppm F and 0.1% Na oxalate was significantly greater than after rinsing with 25 ppm F.

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:-

1. An anti-caries oral hygiene composition in the form of a dentifrice, mouthwash, tablet, lozenge or pastile comprising:

(i) an anti-caries agent consisting essentially of from greater than 0 to 7% by weight of the composition of alkali metal oxalate or alkaline earth oxalate and from 20 to 1500ppm of fluoride ions;

(ii) a dentally acceptable excipient; and

(iii) a pH of from 4 to 10.

2. A composition according to claim 1, in which the alkali metal oxalate and/or alkaline earth metal oxalate is present in an amount of from 0.0025% to 7% by weight.

3. A composition according to claim 1 or 2 in which the alkali metal oxalate or alkaline earth metal oxalate comprises sodium oxalate, potassium oxalate or calcium oxalate or mixtures thereof.

4. A composition according to any one of claims 1 to 3, in which the fluoride ions are derived from an alkali metal fluoride and/or an alkali metal monofluorophosphate.

5. A composition according to any one of claims 1 to 4, which is in the form of a dentifrice.

6. A composition according to any one of claims 1 to 4 which is in the form of a mouthwash.

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7. An oral hygiene composition, substantially as hereinbefore described with reference to the Examples.

DATED THIS 10th January, 1990
DAVIES & COLLISON
Fellows Institute of Patent
Attorneys of Australia.
Patent Attorneys for the Applicant

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