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AUSTRALIA
Patents Act 1990
PATENT REQUEST: STANDARD PATENT

We, COLGATE-PALMOLIVE COMPANY, being the person(s) identified below as the Applicant, request the grant of a standard patent to the person identified below as the Nominated Person, for an invention described in the accompanying complete specification.

Full application details follow.

Applicant: COLGATE-PALMOLIVE COMPANY
a company organized and existing under the laws of the State of Delaware, United States of America

Address: 300 Park Avenue, New York NY 10022, United States of America

Nominated Person: COLGATE-PALMOLIVE COMPANY
a company organized and existing under the laws of the State of Delaware, United States of America

Address: 300 Park Avenue, New York NY 10022, United States of America

Invention Title: "Antibacterial Antiplaque Anticalculus Oral Composition"

Name(s) of Actual Inventor(s): Abdul Gaffar
Nuran Babi
Brian S. Jannone

Address for service is: F.B. RICE & CO.,
28A Montague St,
Balmain N.S.W. 2041

Attorney Code: RI

DIVISIONAL APPLICATION DETAILS

Original application number: 10175/88AJ

We are not an eligible person described in Section 33 - 36 of the Act.

Dated this 27 day of July 1992

COLGATE-PALMOLIVE COMPANY

By:

W. J. Palmer
Registered Patent Attorney



AUSTRALIA
Patents Act 1990

P/OO/OO8
Section 29 (1)
Regulation 3.1(2)

NOTICE OF ENTITLEMENT
(To be filed before acceptance)

I/XX ☒ ROBERT C. SULLIVAN

*being authorised by COLGATE-PALMOLIVE COMPANY

of 300 Park Avenue, New York, New York 10022, United States of
America

the applicant in respect of an application for a patent for an invention entitled
"ANTIBACTERIAL ANTIPLAQUE ANTICALCULUS ORAL COMPOSITION"

filed under Australian Application No. 74235/91, state the following:-

Part 1 - Must be completed for all applications.

The person(s) nominated for the grant of the patent:

☐ *is/*are the actual inventor(s)

or

☐ has, for the following reasons, gained entitlement from the actual inventor(s):
The nominated person is the assignee of the invention from
the actual inventor

Part 2 - Must be completed if the application is a Divisional application.

The person(s) nominated for the grant of the patent *is/*are:

☒ the applicant(s)/patentee(s) of the original application/patent
or

☐ entitled to make a request under Section 113 of the Act in relation to the
original application/patent.

COLGATE-PALMOLIVE COMPANY

Signed: ☒


Robert C. Sullivan

Vice President and Chief Patent Counsel

Date: ☒

FEB 12 1992

Status: ☒

F.B. RICE & CO. PATENT ATTORNEYS

COMMONWEALTH OF AUSTRALIA

Patents Act 1952

APPLICATION FOR A STANDARD PATENT

We, COLGATE-PALMOLIVE COMPANY, of 300 Park Avenue, New York, New York 10022, United States of America, hereby apply for the grant of a Standard Patent for an invention entitled:-

"ANTIBACTERIAL ANTIPLAQUE ANTICALCULUS ORAL COMPOSITION"

which is described in the accompanying complete specification.

This application is made by virtue of Section 51, wherein

Number of original application:- 10175/88

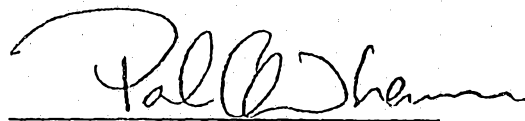
Person by whom made:- COLGATE-PALMOLIVE COMPANY

Our address for service is: F.B. RICE & CO.,
28A Montague St,
Balmain N.S.W. 2041

Dated this 9th day of April 1991

COLGATE-PALMOLIVE COMPANY,

By:

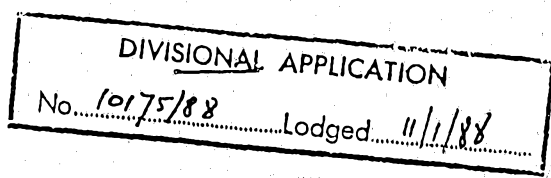


Registered Patent Attorney

TO: The Commissioner of Patents,
COMMONWEALTH OF AUSTRALIA

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(19) AUSTRALIAN PATENT OFFICE (10) Acceptance No. 629742

(54) Title
ANTIBACTERIAL ANTIPLAQUE ANTICALCULUS ORAL COMPOSITION

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(71) Applicant(s)
COLGATE-PALMOLIVE COMPANY

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(57) Claim

1. An oral composition comprising in an orally acceptable vehicle an effective anticalculus amount of an anticalculus material comprising at least one linear molecularly dehydrated polyphosphate salt and an effective antiplaque amount of a substantially water-insoluble non-cationic antibacterial agent which is a benzoate ester.

4. An oral composition as claimed in claim 1 which further comprises sodium fluoride as a fluoride ion source in an amount sufficient to supply 25 to 5000 ppm of fluoride ion.

13. The oral composition as claimed in any one of claims 1 or 4 to 7 which includes a fluoride ion source sufficient to supply 25 to 2000 ppm of fluoride ions and further includes 0.05 to 3% of a water-soluble alkali metal or ammonium synthetic anionic linear polymeric polycarboxylate salt having a molecular weight of 1000 to 1,000,000.

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Patent Act 1952

C O M P L E T E S P E C I F I C A T I O N
(ORIGINAL)

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Application Number :
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Accepted :
Published :

Priority: U.S.A. 008901 dated 30.01.87

Related Art :

Name of Applicant : COLGATE-PALMOLIVE COMPANY

Address of Applicant : 300 Park Avenue, New York, New York
10022, United States of America

Actual Inventor : Abdul Gaffar
 : Nuran Babi
 : Brian S. Jannone

Address for Service : F.B. RICE & CO.,
Patent Attorneys,
28A Montague Street,
BALMAIN. 2041.

Complete Specification for the invention entitled:

"ANTIBACTERIAL ANTIPLAQUE ANTICALCULUS ORAL COMPOSITION"

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

This invention relates to an antibacterial antiplaque anticalculus oral composition. More particularly, it relates to an oral composition containing a polyphosphate anticalculus (that is, antitartar) agent and a compatible
5 antibacterial agent effective to inhibit plaque.

In U.S. Patents 4,627,977 to Gaffar et al; 4,515,772 to Parran et al; and 4,323,551 to Parran, oral compositions are described which include various polyphosphate compounds. In the patent to Gaffar et al, a
10 linear molecular dehydrated polyphosphate salt is employed in conjunction with a fluoride ion-providing source and a synthetic linear polymeric polycarboxylate to inhibit calculus formation.

In the patents to Parran et al and to Parran water
15 soluble dialkali metal pyrophosphate alone or mixed with tetraalkali metal pyrophosphate is employed.

Oral compositions which inhibit calculus formation on dental surfaces are highly desirable since calculus is one of the causitive factors in periodontal conditions. Thus,
20 its reduction promotes oral hygiene.

Dental plaque is a precursor of calculus. Unlike calculus, however, plaque may form on any part of the tooth surface, particularly including at the gingival margin. Hence, besides being unsightly, it is implicated
25 in the occurence of gingivitis.

Accordingly, it would be highly desirable to include antimicrobial agents which have been known to reduce plaque in oral compositions containing anticalculus agents. Indeed, this has been described in U.S. Patent
30 4,022,880 to Vinson et al, wherein a compound providing zinc ions as an anticalculus agent is admixed with an antibacterial agent effective to retard the growth of plaque bacteria. A wide variety of antibacterial agents are described with the zinc

compounds including cationic materials such as guanides and quaternary ammonium compounds as well as non-cationic compounds such as halogenated salicylanilides and halogenated hydroxydiphenyl ethers.

- 5 Hitherto, the cationic antibacterial materials such as chlorhexidine, benzthonium chloride and cetyl pyridinium chloride have been the subject of greatest investigation as antibacterial antiplaque agents. However, in spite of their being used in conjunction with
- 10 zinc anticalculus agent, they are not effective when used with anionic materials such as polyphosphate anticalculus agent. This ineffectiveness is considered to be quite surprising as polyphosphates are chelating agents and the chelating effect has previously been known to increase the
- 15 efficacy of cationic antibacterial agents. (see e.g. Disinfection, Sterilization and Preservation, 2nd Ed., Black, 1977, page 915 and Inhibition and Destruction of the Microbial Cell, Hugo, 1971, page 215). Indeed, quaternary ammonium compound is present in the plaque
- 20 control mouthwash containing pyrophosphate of U.S. Patent 4,323,551 and bis-biguanide antiplaque agent is suggested in the anticalculus pyrophosphate oral composition of U.S. Patent 4,515,772.

- In contrast to the incompatibility of cationic
- 25 antibacterial agents with polyphosphates present as anticalculus agents, the present inventors have found that the noncationic antibacterial agent, benzoate ester, is compatible with polyphosphates present as anticalculus agents. This finding has enabled the production of oral
- 30 compositions containing linear molecularly dehydrated polyphosphate salts and the noncationic antibacterial agent benzoate ester.



Accordingly, the present invention consists in an oral composition comprising in an orally acceptable vehicle an effective anticalculus amount of an anticalculus material comprising at least one linear
5 molecularly dehydrated polyphosphate salt and an effective antiplaque amount of a substantially water-insoluble non-cationic antibacterial agent which is a benzoate ester.

Examples of the benzoate esters which are particularly desirable from considerations of antiplaque
10 effectiveness, safety and formulation are:

Methyl - p-Hydroxybenzoic Acid

Ethyl - p-Hydroxybenzoic Acid

Propyl - p-Hydroxybenzoic Acid

Butyl - p-Hydroxybenzoic Acid

15 The benzoate ester is substantially water-insoluble, meaning that its solubility is less than about 1% by weight in water at 25°C and may be even less than about 0.1%. If an ionizable group is present solubility is determined at a pH at which ionization does not occur.

20 The linear molecularly dehydrated polyphosphate salts operative herein as anticalculus agents are well known, being generally employed in the form of their wholly or partially neutralized water soluble alkali metal (e.g. potassium and preferable sodium) or ammonium salts, and an
25 mixtures thereof. Representative examples include sodium hexametaphosphate, sodium tripolyphosphate, disodium diacid, trisodium monoacid tetrapotassium pyrophosphate and tetrasodium pyrophosphates and the like.



They are generally employed in the instant oral compositions in approximate weight amounts of 0.1 to 7% preferably 0.1 to 7%, more preferably 2 to 7%.

- Particularly desirable anticalculus agents are
- 5 tetraalkali metal pyrophosphates, including mixtures thereof, such as tetrasodium pyrophosphate, tetrapotassium pyrophosphate and mixtures thereof. An anticalculus agent comprising tetrapotassium pyrophosphate and tetrasodium pyrophosphate in a weight ratio of
- 10 tetrapotassium pyrophosphate to tetrasodium pyrophosphate of greater than 1:1 is preferred. An anticalculus agent



~~Particularly desirable anticalculus agents are~~
tetraalkali metal pyrophosphates, including mixtures
thereof, such as ~~tetrasodium pyrophosphate, tetrapotassium~~
~~pyrophosphate and mixtures thereof. An anticalculus agent~~
5 comprising about 4.3% to about 7% by weight of the oral
compositions wherein the weight ratio of tetrapotassium
pyrophosphate to tetrasodium pyrophosphate is from about
4.3:2.7 to about 6:1 is especially preferred.

In order to optimize the anticalculus effectiveness
10 of the oral composition, inhibitors against enzymatic
hydrolysis of the polyphosphate are desirably present.
Such agents are an amount of a fluoride ion source
sufficient to supply 25 ppm. to 5,000 ppm. of fluoride
ions, and 0% to 3% of a synthetic anionic polymeric
15 polycarboxylate having a molecular weight of about 1,000
to about 1,000,000, preferably about 30,000 to about
500,000.

The sources of fluoride ions, or fluorine-providing
component, as acid phosphatase and pyrophosphatase enzyme
20 inhibitor component, are well known in the art as
anti-carries agents. These compounds may be slightly
soluble in water or may be fully water-soluble. They are
characterized by their ability to release fluoride ions in
water and by freedom from undesired reaction with other
25 compounds of the oral preparation. Among these materials
are inorganic fluoride salts, such as soluble alkali
metal, alkaline earth metal salts, for example, sodium
fluoride, potassium fluoride, ammonium fluoride, calcium
fluoride, a copper fluoride such as cuprous fluoride, zinc
30 fluoride, barium fluoride, sodium fluorosilicate, ammonium
fluorosilicate, sodium fluoroaluminum silicate, sodium
fluoroaluminum phosphate, sodium monofluorophosphate, aluminum
mono- and di-fluorophosphate, and fluorinated sodium
calcium pyrophosphate. Alkali metal and tin fluorides,
35 such as sodium and stannous fluorides, sodium
monofluorophosphate (MFP) and mixtures thereof, are
preferred.



The amount of fluorine-providing compound is dependent to some extent upon the type of compound, its solubility, and the type of oral preparation, but it must be a non-toxic amount, generally about 0.005 to about 3.0% in the preparation. In a dentifrice preparation, e.g. dental gel, toothpaste (including cream), toothpowder, or dental tablet, an amount of such compound which releases up to about 5,000 ppm of F ion by weight of the preparation is considered satisfactory. Any suitable minimum amount of such compound may be used, but it is preferable to employ sufficient compound to release about 300 to 2,000 ppm, more
10 preferable about 800 to about 1,500 ppm of fluoride ion.

Typically, in the cases of alkali metal fluorides, this component is present in an amount up to about 2% by weight, based on the weight of the preparation, and preferably in the range of about 0.01% to 1%. In the case of sodium monofluorophosphate, the compound may be present in an amount of about 0.1-3%, more typically about 0.76%.

In dentifrice preparations such as lozenges and chewing gum, the fluorine-providing compound is typically present in an amount sufficient to release up to about 500 ppm, preferably about 25 to 300
20 ppm by weight of fluoride ion. Generally about 0.005 to about 1.0 wt. % of such compound is present.

^{Synthetic}
~~The synthetic~~ anionic polymeric polycarboxylate is an inhibitor of alkaline phosphatase enzyme. Synthetic anionic polymeric polycarboxylates and their complexes with various cationic germicides, zinc and magnesium have been previously disclosed as anticalculus agents per se in, for example U.S. Patent No. 3,429,963 to Shedlovsky; U.S. Patent No 4,152,420 to Gaffar; U.S. Patent No. 3,956,480 to Dichter et al; U.S. Patent No. 4,138,477 to Gaffar; and U.S. Patent No. 4,183,914 to Gaffar et al. However, only in aforementioned U.S. Patent 4,627,977



to Gaffar et al is there disclosed use of such polycarboxylates alone for inhibiting salivary hydrolysis of pyrophosphate anticalculus agents, much less in combination with a compound providing a source of fluoride ion. It is to be understood that the synthetic anionic polymeric polycarboxylates so disclosed in these several patents are operative in the compositions and methods of this invention and such disclosures are to that extent incorporated herein by reference thereto.

The synthetic anionic polymeric polycarboxylates optionally but preferably employed herein are, as indicated above, well known, being
10 often employed in the form of their free acids or preferably partially or more preferably fully neutralized water soluble alkali metal (e.g. potassium and preferably sodium) or ammonium salts. Preferred are 1:4 to 4:1 copolymers of maleic anhydride or acid with another polymerizable ethylenically unsaturated monomer, preferably methyl vinyl ether (maleic anhydride) having a molecular weight (M.W.) of about 30,000 to about 1,000,000. These copolymers are available for example as Gantrez (AN 139 (M.W. 500,000), A.N. 119 (M.W. 250,000); and preferably S-97 Pharmaceutical Grade (M.W. 70,000), of GAF Corporation. The term
20 "synthetic" is intended to exclude known thickening or gelling agents comprising carboxymethylcellulose and other derivatives of cellulose and natural gums.

Other operative polymeric polycarboxylates include those disclosed in U.S. Patent No. 3,956,480 referred to above, such as the 1:1 copolymers of maleic anhydride with ethyl acrylate, hydroxyethyl methacrylate, N-vinyl-2-pyrrolidone, or ethylene, the latter being available for example as Monsanto EMA No. 1103, M.W. 10,000 and EMA Grade 61, and 1:1 copolymers of acrylic acid with methyl or hydroxyethyl methacrylate, methyl or ethyl acrylate, isobutyl vinyl ether or N-vinyl-2-pyrrolidone.



Additional operative polymeric polycarboxylates disclosed in above referred to U.S. Patent No. 4,138,477 and 4,183,914, include copolymers of maleic anhydride with styrene, isobutylene or ethyl vinyl ether, polyacrylic, polyitaconic and polymaleic acids, and sulfoacrylic oligomers of M.W. as low as 1,000, available as Uniroyal ND-2.

Suitable generally are polymerized olefinically or ethylenically unsaturated carboxylic acids containing an activated carbon-to-carbon olefinic double bond and at least one carboxyl group, that is, an acid containing an olefinic double bond which readily
10 functions in polymerization because of its presence in the monomer molecule either in the alpha-beta position with respect to a carboxyl group or as part of a terminal methylene grouping. Illustrative of such acids are acrylic, methacrylic, ethacrylic, alpha-chloroacrylic, crotonic, beta-acryloxy propionic, sorbic, alpha-chlorsorbic, cinnamic, beta-styrylacrylic, muconic, itaconic, citraconic, mesaconic, glutaconic, aconitic, alpha-phenylacrylic, 2-benzyl acrylic, 2-cyclohexylacrylic, angelic, umbellic, fumaric, maleic acids and anhydrides. Other different olefinic monomers copolymerizable with such
20 carboxylic monomers include vinylacetate, vinyl chloride, dimethyl maleate and the like. Copolymers contain sufficient carboxylic salt groups for water-solubility.

Also useful herein are so-called carboxyvinyl polymers disclosed as toothpaste components in U.S. 3,980,767 to Chown et al; U.S. 3,935,306 to Roberts et al; U.S. 3,919,409 to Perla et al; U.S. 3,911,904 to Harrison, and U.S. 3,711,604 to Colodney et al. They are commercially available for example under the trademarks Carbopol 934, 940 and 941 of B. F. Goodrich, these products consisting essentially of a colloiddally water-soluble polymer of polyacrylic acid crosslinked with from about 0.75% to about 2.0% of polyallyl sucrose or polyallyl
30 pentaerythritol as cross linking agent.



The synthetic anionic polymeric polycarboxylate component is mainly a hydrocarbon with optional halogen and O-containing substituents and linkages as present in for example ester, ether and OH groups, and when present is generally employed in the instant compositions in approximate weight amounts of 0.05 to 3%, preferably 0.05 to 2%, more preferably 0.1 to 2%. Amounts in the upper portions of these ranges are typically employed in dentifrice compositions typically containing a dental abrasive and used in conjunction with brushing of the teeth, e.g. tooth pastes (including creams), gels, powders and tablets. Amounts in excess of these ranges may be employed for thickening or gelling purposes.

As indicated above, these polymeric polycarboxylates have been found to be effective inhibitors of alkaline phosphatase enzyme. Since this enzyme has little activity (for hydrolyzing pyrophosphate) at about pH 7.0 or below, the polymeric polycarboxylate component may, if desired, be omitted from oral preparations formulated to operate at such pH of 7.0 or below. Such omission however could reduce the versatility and anticalculus effectiveness of the present oral compositions over the broad pH range of about 4.5 to about 10.

In oral preparations such as mouthwashes, lozenges and chewing gum, the fluorine-providing compound may be typically present in an amount sufficient to release up to about 500 ppm, preferably about 25 to about 300 ppm by weight of fluoride ion. Generally about 0.005 to about 1.0 wt.% of such compound is present.

In certain ~~highly preferred~~ forms of the invention the oral composition may be substantially liquid in character, such as a mouthwash or rinse. In such a preparation the vehicle is typically a water-alcohol mixture desirably including a humectant as described below. Generally, the weight ratio of water to alcohol is in the range



of from about 1:1 to about 20:1, preferably about 3:1 to 10:1 and more preferably about 4:1 to about 6:1. The total amount of water-alcohol mixture in this type of preparation is typically in the range of from about 70 to about 99.9% by weight of the preparation. The alcohol is typically ethanol or isopropanol. Ethanol is preferred.

10 The pH of such liquid and other preparations of the invention is generally in the range of from about 4.5 to about 9 and typically from about 5.5 to 8. The pH is preferably in the range of from about 6 to about 8.0. It is noteworthy that the compositions of the invention may be applied orally at a pH below 5 without substantially decalcifying or otherwise damaging dental enamel. The pH can be controlled with acid (e.g. citric acid or benzoic acid) or base (e.g. sodium hydroxide) or buffered (as with sodium citrate, benzoate, carbonate, or bicarbonate, disodium hydrogen phosphate, sodium dihydrogen phosphate, etc.).

20 In certain other desirable forms of this invention, the oral composition may be substantially solid or pasty in character, such as toothpowder, a dental tablet or a dentifrice, that is a toothpaste (dental cream) or gel dentifrice. The vehicle of such solid or pasty oral preparations generally contains dentally acceptable polishing material. Examples of polishing materials are water-insoluble sodium metaphosphate, potassium metaphosphate, tricalcium phosphate, dihydrated calcium phosphate, anhydrous dicalcium phosphate, calcium pyrophosphate, magnesium orthophosphate, trimagnesium phosphate, calcium carbonate, aluminum silicate, zirconium silicate, silica, bentonite, and mixtures thereof. Other suitable polishing material include the particulate thermosetting resins described in U.S. Pat. No. 3,070,510 of Dec. 15, 1962 such as melamine-, phenolic, and urea-formaldehydes, and cross-linked polyepoxides and polyesters. Preferred polishing materials include crystalline silica having particle sized of up to about 5



microns, a mean particle size of up to about 1.1 microns, and a surface area of up to about 50, 000 cm.²/gm., silica gel or colloidal silica, and complex amorphous alkali metal aluminosilicate.

When visually clear gels are employed, a polishing agent of colloidal silica, such as those sold under the trademark SYLOID as Syloid 72 and Syloid 74 or under the trademark SANTOCEL as Santocel 100 alkali metal almuino-silicate complexes are particularly useful, since they have refractive indices close to the refractive indices of gelling agent-liquid (including water and/or humectant) systems commonly used in
10 dentifices.

Many of the so-called "water-insoluble" polishing materials are anionic in character and also include small amounts of soluble material. Thus, insoluble sodium metaphosphate may be formed in any suitable manner as illustrated by Thorpe's Dictionary of Applied Chemistry, Volume 9, 4th Edition, pp. 510-511. The forms of insoluble sodium metaphosphate known as Madrell's salt and Kurrol's salt are further examples of suitable materials. These metaphosphate salts exhibit only a minute solubility in water, and therefore are commonly referred to as insoluble metaphosphates (IMP). There is present therein a minor amount
20 of soluble phosphate material as impurities, usually a few percent such as up to 4% by weight. The amount of soluble phosphate material, which is believed to include a soluble sodium trimetaphosphate in the case of insoluble metaphosphate, may be reduced or eliminated by washing with water if desired. The insoluble alkali metal metaphosphate is typically employed in powder form of a particle size such that no more than 1% of the material is larger than 37 microns.

The polishing material is generally present in the solid or pasty compositions in weight concentrations of about 10% to about 99%. Preferably, it is present in amounts ranging from about 10% to about 75%



in toothpaste, and from about 70% to about 99% in toothpowder.

In a toothpaste, the liquid vehicle may comprise water and humectant typically in an amount ranging from about 10% to about 80% by weight of the preparation. Glycerine, propylene glycol, sorbitol, polypropylene glycol and/or polyethylene glycol (e.g. 400-600) exemplify suitable humectants/carriers. Also advantageous are liquid mixtures of water, glycerine and sorbitol. In clear gels where the refractive index is an important consideration, about 3-30 wt. % of water, 0 to about 70 wt.% of glycerine and about 20-80 wt. % of sorbitol are preferably employed.

10

Toothpastes, creams and gels typically contain a natural or synthetic thickener or gelling agent in proportions of about 0.1 to about 10, preferably about 0.5 to about 5wt.%. A suitable thickener is synthetic hectorite, a synthetic colloidal magnesium alkali metal silicate complex clay available for example as Laponite (e.g. CP, SP 2002,D) marketed by Laporte Industries Limited. Laponite D analysis shows, approximately by weight, 58.00% SiO_2 , 25.40% MgO , 3.05% Na_2O , 0.98% Li_2O , and some water and trace metals. Its true specific gravity is 2.53 and it has an apparent bulk density (g./ml. at 8% moisture) of 1.0.

20

Other suitable thickeners include Irish moss, gum tragacanth, starch, polyvinylpyrrolidone, hydroxyethylpropylcellulose, hydroxybutyl methyl cellulose, hydroxypropyl methyl cellulose, hydroxyethyl cellulose (e.g. available as Natrosol), sodium carboxymethyl cellulose, and colloidal silica such as finely ground Syloid (e.g. 244).

It will be understood that, as is conventional, the oral preparations are to be sold or otherwise distributed in suitable labelled packages. Thus a jar of mouthrinse will have a label describing it, in substance, as a mouthrinse or mouthwash and having



directions for its use; and a toothpaste, cream or gel will usually be in a collapsible tube, typically aluminum, lined lead or plastic, or other squeeze, pump or pressurized dispenser for metering out the contents, having a label describing it, in substance, as a toothpaste, gel or dental cream.

Organic surface-active agents are used in the compositions of the present invention to achieve increased prophylactic action, assist in achieving thorough and complete dispersion of the anticalculus agent throughout the oral cavity, and render the instant compositions more
10 cosmetically acceptable. The organic surface-active material is preferably anionic, nonionic or ampholytic in nature, and it is preferred to employ as the surface-active agent a deterative material which imparts to the composition deterative and foaming properties. Suitable examples of anionic surfactants are water-soluble salts of higher fatty acid monoglyceride monosulfates, such as the sodium salt of the monosulfated monoglyceride of hydrogenated coconut oil fatty acids, higher alkyl sulfates such as sodium lauryl sulfate, alkyl aryl sulfonates such as sodium dodecyl benzene sulfonate, higher alkyl sulfoacetates, higher fatty acid esters of 1,2-dihydroxy propane
20 sulfonate, and the substantially saturated higher aliphatic acyl amides of lower aliphatic amino carboxylic acid compounds, such as those having 12 to 16 carbons in the fatty acid, alkyl or acyl radicals, and the like. Examples of the last mentioned amides are N-lauroyl sarcosine, and the sodium, potassium, and ethanolamine salts of N-lauroyl, N-myristoyl, or N-palmitoyl sarcosine which should be substantially free from soap or similar higher fatty acid material. The use of these sarcosinate compounds in the oral compositions of the present invention is particularly advantageous since these materials exhibit a prolonged and marked effect in the inhibition of acid formation in the oral cavity



due to carbohydrate breakdown in addition to exerting some reduction in the solubility of tooth enamel in acid solutions. Examples of water-soluble nonionic surfactants are condensation products of ethylene oxide with various reactive hydrogen-containing compounds reactive therewith having long hydrophobic chains (e.g. aliphatic chains of about 12 to 20 carbon atoms), which condensation products ("ethoxamers") contain hydrophilic polyoxyethylene moieties, such as condensation products of poly (ethylene oxide) with fatty acids, fatty alcohols, fatty amides, polyhydric alcohols (e.g. sobitan monostearate) and polypropyleneoxide (e.g. Pluronic materials). It is preferred to use from about 1.0 - 2.0% by weight of the foregoing surface active materials in the instant compositions.



Various other materials may be incorporated in the oral preparations of this invention such as whitening agents, preservatives, silicones, chlorophyll compounds and/or ammoniated material such as urea, diammonium phosphate, and mixtures thereof. These adjuvants, where present, are incorporated in the preparations in amounts which do not substantially adversely affect the properties and characteristics desired. Significant amounts of zinc, magnesium and other metal salts and materials, generally soluble, which would complex with active components of the instant invention are to be avoided.

Any suitable flavoring or sweetening material may also be employed. Examples of suitable flavoring constituents are flavoring oils, e.g. oil of spearmint, peppermint, wintergreen, sassafras, clove, sage, eucalyptus, marjoram, cinnamon, lemon, and orange, and methyl salicylate. Suitable sweetening agents include sucrose, lactose, maltose, sorbitol, xylitol, sodium cyclamate, perillartine, AMP (aspartyl phenyl alanine, methyl ester), saccharine and the like. Suitably, flavor and sweetening agents may together comprise from about 0.1% to 5% more of the preparation.

In the preferred practice of this invention an oral composition



according to this invention such as a mouthwash or
dentifrice containing the composition of the present
invention is preferably applied regularly to dental
enamel, such as every day or every second or third day or
5 preferably from 1 to 3 times daily, at a pH of about 4.5
to about 9, generally about 5.5 to about 8, preferably
about 6 to 8, for at least 2 weeks up to 8 weeks or more
up to lifetime.

The compositions of this invention can be
10 incorporated in lozenges, or in chewing gum or other
products, e.g. by stirring into a warm gum base or coating
the outer surface of a gum base, illustrative of which may
be mentioned jelutone, rubber latex, vinylite resins,
etc., desirably with conventional plasticizers or
15 softeners, sugar or other sweeteners or carbohydrates such
as glucose, sorbitol and the like.

The following examples are further illustrative of
the nature of the present invention, but it is understood
that the invention is not limited thereto. All amounts
20 and proportions referred to herein and in the appended
claims are by weight.



Example 1

Slurries and solutions described below are prepared to determine effectiveness in terms of minimum inhibitory concentration (MIC) of various antibacterial agents against a variety of oral bacterial organisms implicated in formation of plaque and leading to gingivitis on dental surfaces. Soft plaque contains about 1.7×10^{11} organism/gm. (net weight). The antibacterial agents are admixed with anionic materials, particularly anionic surface active agent often commonly employed in oral compositions and polyphosphate anticalculus agent.

10 Minimum inhibitory concentration (MIC) of antibacterial agent is used to evaluate the efficacy of the agent in vitro. MIC is defined as the minimum concentration in micrograms/ml of antibacterial agent at which the growth of bacteria is completely inhibited by the agent. The smaller the MIC value the greater is the efficacy of the antibacterial agent to inhibit the growth of the bacteria. The in vitro MIC data is related to the efficacy of the dentifrice in vivo since retention and release of antibacterial agent into the oral cavity after toothbrushing is in the range of mcg/ml.

20 In the Tables, following disclosure and following Examples, the agent Triclosan, 2,4,4'-trichloro-2'-hydroxydiphenyl ether is indicated as "TCHE"; the quaternary ammonium antibacterial agents benzthonium chloride is indicated as "BTC"; The biguanide chlorhexidine digluconate is indicated as "CH", sodium lauryl sulfate is indicated as "SLS"; the copolymer of maleic anhydride and methyl vinyl ether available from GAF corporation as "Gantrez S-97" is identified as "Gantrez"; tetrasodium pyrophosphate is identified as "pyrophosphate"; and sodium fluoride is identified as "NaF".



TABLE 1

Test Solution	Minimum Inhibition Concentration (MIC) in mcg/ml			
	<u>Bacteriodes gingivalis</u>	<u>Bacteriodes intermedius</u>	<u>Actinobacillus actinomycetem- comitans</u>	<u>Streptococcus mutans</u>
10 1. 0.5% TCHE and 1% SLS in water	2.5	2.5	5.0	25.0
2. 0.5% TCHE, 1% SLS, 1% Gantrez, 2% Pyrophosphate and 0.2% NaF in water	2.5	2.5	5.0	25.0
3. 1% SLS in water	NE	NE	NE	NE
20 4. 1% SLS, 1% Gantrez and 2% Pyrophosphate in water	NE	NE	NE	NE

note: NE = not effective

The results indicate that TCHE in the presence of anionic surfactant inhibited four dental plaque organisms, Bacteriodes gingivalis, Bacteriodes intermedius, Actinobacillus actinomycetemcomitans and Strep. mutans at 2.5 mcg/ml and 2.5 mcg/ml, 5.0 mcg/ml and 25.0 mcg/ml respectively(1). Similar antibacterial effect is seen in the presence of Gantrez/pyrophosphate/fluoride(2).
30 SLS per se and a combination of SLS/Gantrez/pyrophosphate/fluoride was ineffective (3 and 4).

It is noteworthy that in human clinical tests with cationic antibacterial agents, 0.075% BTC dissolved in water is effective in reducing plaque formation while 0.075% BTC and 1% pyrophosphate dissolved in water is not. Similarly, 0.01% CH dissolved in water is effective in reducing plaque formation while 0.01% CH and 1% sodium N-lauroyl sarcosinate dissolved in water is not.



Example 2

The adsorption to and release from tooth minerals for antiplaque/ antitartar efficacy of agents is assessed by adsorption of antibacterial agent to saliva coated tooth mineral hydroxyapatite in the presence and the absence of pyrophosphate (soluble tetrasodium pyrophosphate)/ Gantrez/NaF.

200 mg. of hydroxyapatite (HA) is treated with human saliva for 2 hours. The excess saliva is washed off with a buffer and saliva coated HA is used for adsorption studies. Various concentrations of TCHE in SLS or in SLS/ pyrophosphate/Gantrez/NaF are mixed with the coated HA and incubated at 37° for 3 hours under continuous agitation. At the end of incubation period, the mixtures are centrifuged, HA separated and the amounts of TCHE adsorbed determined by estimating TCHE in the supernatant at 283nm in a Gilford spectrophotometer. The amounts adsorbed are calculated by the difference between the amount added and the amount left in the supernatant after the incubation with coated HA. The table below summarizes the data.



TABLE 2

<u>Components and Concentrations</u>	<u>% of TCHE Adsorbed to Coated HA</u>
0.005% TCHE in 1% SLS	80%
0.01% TCHE in 1% SLS	85%
0.015% TCHE in 1% SLS	85%
0.02% TCHE in 1% SLS	38%
0.005% TCHE in 1% SLS; 0.5% Gantrez; 2% pyrophosphate/ 0.24% NaF	80%
10 0.01% TCHE "	85%
0.015% TCHE "	86%
0.02% TCHE "	87%

The data indicates that the addition of pyrophosphate/
Gantrez/NaF does not impair adsorption of TCHE to saliva coated tooth
minerals.



Example 3

<u>Dentifrice Compositions</u>	<u>A</u>	<u>B</u>	<u>C</u>
	<u>Parts</u>	<u>Parts</u>	<u>Parts</u>
Glycerine	15.00	10.20	15.00
Polyethylene Glycol 600	5.00	3.00	5.00
Iota Carrageenan	0.60	-	0.60
Sodium Carboxymethyl Cellulose	-	1.00	-
Sodium Saccharin	0.40	-	0.40
Sodium Cyclamate	-	3.00	-
10 Sodium Fluoride	0.243	0.243	0.243
Deionized water	15.08	29.907	23.657
Titanium Dioxide	-	-	0.50
Sodium Benzoate	-	0.50	-
FD&C Blue No. 1(1% Solution)	0.400	-	-
Sorbitol (70%)	19.807	22.50	22.50
Gantrez S-97	8.330(*)	1.00(**)	1.00(**)
Tetrasodium Pyrophosphate	1.50	1.50	1.50
Tetrapotassium Pyrophosphate	4.50	4.50	4.50
Preciphated Amorph. Hydrated Silica	16.00	19.50	-
20 Preciphated Amorp. Silica containing combined alumina	-	-	16.00
Silica Thickener	7.00	-	5.50
Flavor	1.10	0.95	1.10
Sodium Lauryl Sulfate	1.20	1.20	1.20
TCHE	0.50	0.50	0.50

* liquid

** powder



Example 4

The dentifrice described in Example 3A is compared with the same composition except without any TCHE and with added 0.50 parts of water. Aqueous extracts of each dentifrice are prepared as follows: 50 ml of distilled water is added to 1.0 gm of each dentifrice, mixed well for a couple of hours with stirring bar and centrifuged, after which the supernatant is collected as aqueous extract. Antibacterial activity of the dentifrice extracts are evaluated on Bacteriodes gingivalis. Results are summarized below.

10

TABLE 3

<u>Treatment</u>	<u>Inhibition of Growth of <i>Bacteriodes gingivalis</i></u>
Extract from dentifrice containing TCHE (1:500)	100.0
Extract from dentifrice without TCHE (1:500)	0.0
TCHE (5.0 mcg/ml) by itself	100.0

20 These results indicate that TCHE antibacterial antiplaque agent is compatible in a dentifrice composition containing anionic surfactant plus pyrophosphate anticalculus ingredients with enzyme inhibitors Gantrez and NaF. Similar comparable effects prevail when each of hexyl resorcinol, 2,2'-methylene bis(4-chloro-6-bromophenol) and ~~Fluorophene~~ replace TCHE.



Example 5

	<u>Mouthrinse</u>	<u>Parts</u>
	Tetrasodium Pyrophosphate	2.00
	Gantrez S-97	0.25
5	Glycerine	10.00
	Sodium Fluoride	0.05
	Pluronic F108	2.00
	(Polyoxyethylene/Polyoxypropylene Block Copolymer)	
10	TCHE	0.10
	Flavor	0.40
	Water	Q.S. to 100.00

Example 6

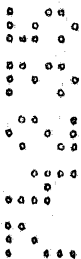
	<u>Lozenge</u>
15	75-80% Sugar
	1-20% Corn Syrup
	0.1-1.0 Flavor
	2% Tetrasodium Pyrophosphate
	0.25% Gantrez S-97
20	0.01 to 0.05% NaF
	0.01 to 0.1% TCHE
	1 to 5% Magnesium Stearate Lubricant
	0.01 to 0.2% Water



Example 7

<u>Chewing Gum</u>	<u>Parts</u>
Gum base	25.00
Sorbitol (70%)	17.00
TCHE	0.50 to 0.10
Tetrasodium Pyrophosphate	2.00
Gantrez S.97	0.25
NaF	0.05
Glycerine	0.50
10 Crystalline Sorbitol	53.00
Flavor and Water	Q.S. to 100.00

This invention has been described with respect to certain preferred embodiments and it will be understood that modifications and variations thereof obvious to those skilled in the art are to be included within the purview of this application and the scope of the appended claims.



THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:-

1. An oral composition comprising in an orally acceptable vehicle an effective anticalculus amount of an anticalculus material comprising at least one linear
5 molecularly dehydrated polyphosphate salt and an effective antiplaque amount of a substantially water-insoluble non-cationic antibacterial agent which is a benzoate ester.
2. An oral composition as claimed in claim 1 wherein the anticalculus material is a mixture of tetrasodium
10 pyrophosphate and tetrapotassium pyrophosphate salts.
3. An oral composition as claimed in claim 1 wherein the anticalculus material is at least one wholly or partially neutralized water-soluble alkali metal or ammonium tripolyphosphate or hexametaphosphate salt.
- 15 4. An oral composition as claimed in claim 1 which further comprises sodium fluoride as a fluoride ion source in an amount sufficient to supply 25 to 5000 ppm of fluoride ion.
5. An oral composition as claimed in any one of the
20 preceding claims wherein the anticalculus material is present in an amount of between 2% and 7% by weight.
6. An oral composition as claimed in any one of the preceding claims wherein the benzoate ester is present in an amount of between 0.01 and 5% by weight.
- 25 7. An oral composition as claimed in any one of the preceding claims wherein the anticalculus material is present in an amount of between 4.3 and 7% by weight.
8. The oral composition as claimed in claim 2 or any one of claims 5 to 7 when dependent on claim 2 wherein the
30 tetrapotassium pyrophosphate and the tetrasodium pyrophosphate are present in a weight ratio of tetrapotassium pyrophosphate to tetrasodium pyrophosphate of greater than 1:1.
9. An oral composition as claimed in claim 2 or any one
35 of claims 5 to 8 when dependent on claim 2 wherein the



tetrapotassium pyrophosphate and the tetrasodium pyrophosphate are present in a weight ratio of from 4.3:2.7 to 6:1.

10. The oral composition as claimed in claim 3 wherein
5 the anticalculus material is present in an amount of substantially 0.1 to 7% by weight and the antibacterial agent is present in an amount of substantially 0.01 to 5% by weight.

11. The oral composition as claimed in claim 11 wherein
10 the anticalculus material is sodium tripolyphosphate.

12. The oral composition as claimed in claim 11 wherein the anticalculus material is sodium hexametaphosphate.

13. The oral composition as claimed in any one of
15 claims 1 or 4 to 7 which includes a fluoride ion source sufficient to supply 25 to 2000 ppm of fluoride ions and further includes 0.05 to 3% of a water-soluble alkali metal or ammonium synthetic anionic linear polymeric polycarboxylate salt having a molecular weight of 1000 to 1,000,000.

20 14. The oral composition as claimed in claim 13 wherein the fluoride ion source is in an amount sufficient to supply 300 to 2000 ppm of fluoride ions and the polycarboxylate salt is 0.1 to 2% of a water-soluble alkali metal or ammonium salt of a copolymer of vinyl
25 methyl ether and maleic acid or anhydride having a molecular weight of 30,000 to 500,000.

15. The oral composition as claimed in any one of the preceding claims which further contains a dentally acceptable water-insoluble polishing agent and the oral
30 composition is a tooth powder, dental tablet, toothpaste or dentifrice.

16. The oral composition as claimed in claim 15 wherein the oral composition contains substantially 10 to 80% by weight of a liquid phase comprising water and humectant,
35 substantially 0.1 to 10% by weight of a gelling agent and



substantially 10 to 75% by weight of the polishing agent and the oral composition is a toothpaste or gel dentifrice.

17. The oral composition as claimed in either one of claims 15 or 16 wherein the polishing agent is a silica
5 polishing material.

18. The oral composition as claimed in claim 17 wherein the oral composition contains 70 to 99% by weight of the polishing material and the oral composition is a toothpowder.

10 19. The oral composition as claimed in any one of claims 1 to 14 wherein the oral composition contains substantially 70 to 99.9% by weight of a mixture of water and alcohol in a weight ratio of from substantially 1:1 to substantially 20:1 and the oral composition is a mouth
15 rinse.

20. The oral composition as claimed in claim 19 wherein the alcohol is ethanol.

21. The oral composition as claimed in any one of claims 1 to 14 wherein the oral composition is in the form
20 of a lozenge.

22. The oral composition as claimed in any one of claims 1 to 14 wherein the oral composition is in the form of a chewing gum.

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