Description

This invention relates to oral compositions containing an anticalculus agent.

Calculus is a hard, mineralized formation which forms on the teeth. Regular brushing aids in preventing a rapid buildup of these deposits, but even regular brushing is not sufficient to remove all of the calculus deposits which adhere to the teeth. Calculus is formed on the teeth when crystals of calcium phosphates begin to be deposited in the pellicle and extracellular matrix of the dental plaque and become sufficiently closely packed together for the aggregates to become resistant to deformation. There is no complete agreement on the route by which calcium and orthophosphate ultimately become the crystalline material called hydroxyapatite (HAP). It is generally agreed, however, that at higher saturations, that is, above the critical saturation limit, the precursor to crystalline HAP is an amorphous or microcrystalline calcium phosphate. "amorphous calcium phosphate" although related to hydroxyapatite differs from it in atomic structure, particle morphology, and stoichiometry. The X-ray diffraction pattern of amorphous calcium phosphate shows broad peaks typical of amorphous materials, which lack the long-range atomic order characteristic of all crystalline materials, including HAP. It is apparent, therefore, that agents which effectively interfere with crystalline growth of HAP will be effective as anticalculus agents. A suggested mechanism by which the anticalculus agents of this invention inhibit calculus formation probably involves an increase of the activation energy barrier, thus inhibiting the transformation of precursor amorphous calcium phosphate to HAP.

Studies have shown that there is a good correlation between the ability of a compound to prevent HAP crystalline growth in vitro and its ability to prevent calcification in vivo, provided of course that such compound is stable in and inert to saliva and its components.

It is well known in the art that water soluble hexametaphosphates, tripolyphosphates and pyrophosphates and the like are effective calcium and magnesium ion suppressors, inhibitors, seguestrants and/or chelating agents, and are effective inhibitors of HAP formation in vitro. U.S. Pat. No. 4,515,772 issued May 7, 1985, to Parran et al. discloses and claims oral anticalculus compositions containing a fluoride ion source and soluble dialkali metal pyrophosphates. The voluminous number of acknowledged prior art and "References Cited" in this patent indicate the many uses and functions of polyphosphates hitherto proposed in oral compositions.

However, as in part admitted in the aforesaid patent disclosure and as shown hereinafter in U.S. Patent 4,627,877, issued December 9, 1986, to Gaffar et al. as well as and in U.S. Patent 4,806,340, issued February 21, 1989, to Gaffar et al., the linear molecularly dehydrated polyphosphates (i.e. hexametaphosphates, tripolyphosphates, pyrophosphates, etc.) in common, when introduced into the oral cavity and/or saliva are significantly hydrolyzed by salivary enzymes (phosphatase) to orthophosphates which are ineffective as inhibitors of HAP formation.

In U.S. Patents 4,627,977 and 4,806,340, the use of polymeric polycarboxylate and of a fluoride ion-source was taught to successfully overcome the hydrolysis of the linear molecularly dehydrated polyphosphate anticalculus agents by salivary phosphatase. Thus, polycarboxylate inhibits pyrophosphate hydrolyses by alkaline phosphatase; the fluoride-ion source inhibits pyrophosphate hydrolysis by acid phosphatase and pyrophosphatase.

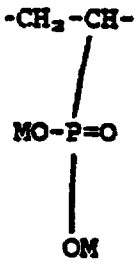
It is an object of the present invention to even more effectively inhibit the action of salivary enzymes on polyphosphate anticalculus agents with a non-polycarboxylate polymer.

A further object of the invention is to provide an oral composition which inhibits the transformation of amorphous calcium phosphate to HAP crystal structure normally associated with calculus.

Another object of this invention is the provision of an improved method for inhibiting the formation of calculus.

Other objects and advantages will appear as the description process.

In accordance with certain of its aspects, this invention relates to an oral composition containing, in an orally acceptable vehicle an effective anticalculus amount of at least one linear molecularly dehydrated polyphosphate salt as essential anticalculus agent, and, an effective amount of inhibitor against enzymatic hydrolysis of said agent in saliva, eg up to about 4% of a synthetic anionic polyvinyl phosphonate, having recurring groups



and an average molecular weight of at least about 1,000 and greater; wherein M and M^1 represent a hydrogen atom or an alkali metal of ammonium grou, and wherein M and M^1 are tje same of different.

Molecular weight values given for such polyvinyl phosphonates are obtained from viscosity or light scattering measurements. Synthetic anionic polyvinyl phosphonates have been previously disclosed as anticalculus agents per se in, U.S. Patent No. 3,429,963 to Shedlovsky. However, that patent does not disclose use of such polyvinyl phosphonate agent for inhibiting salivary hydrolysis of linear polyphosphates.

The linear molecularly dehydrated polyphosphate salts, such as hexametaphosphates, tripolyphosphates and pyrophosphates, which are 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 or sodium) or ammonium salts, and any mixtures thereof. Representative examples include sodium hexametaphosphate, sodium tripolyphosphate, disodium diacid pyrophosphate, trisodium monoacid pyrophosphate and tetrasodium pyrophosphate and the like; for instance the linear molecularly dehydrated polyphosphates may contain about 2 to 125 phosphorus atoms. They are generally employed in the instant oral compositions in approximate weight amounts of about 0.1 to 7% preferably about 2 to 6%. As previously indicated, these salts are disclosed as anticalculus agents in U.S. Patent Nos. 4,627,977 and 4,806,340.

When pyrophosphate salt is employed it is preferred to use a mixture of tetrapotassium pyrophosphate and tetrasodium pyrophosphate, with tetrapotassium pyrophosphate being in predominant amount. When only tetrasodium pyrophosphate is employed, some can remain undissolved, thereby rendering the oral composition gritty in appearance and feel. Thus, when a preferred combination of about 4.3-7% by weight of a mixture of tetrapotassium pyrophosphate and tetrasodium pyrophosphate is employed, the tetrapotassium pyrophosphate salt is in predominant amount and grittiness is substantially reduced. Preferred ratios of the tetrapotassium-tetrasodium salts range from about 4.3:2.7 to about 6:1, especially a ratio of 4.5:1.5. There may be desirably present about 4.3% to about 7% of tetrapotassium pyrophosphate alone or with up to 2.7% of tetrasodium pyrophosphate. In an alternative preferred embodiment lesser effective anticalculus amounts of tetrasodium pyrophosphate, such as about 0.1-2% by weight are employed and effectively dissolved. An aspect of the invention also includes the presence of, dialkali metal pyrophosphate, for instance in amount of about 0.1% to about 0.4% or about 1.0% by weight if desired.

The polyvinylphosphonate may be present as its water-soluble acid form, or salt (including acid salts) form. Salts include the alkali metal, preferably sodium or potassium, or ammonium water-soluble salts.. The polymer has an average molecular weight of at least about 1,000, typically about 1,000 to about 1,000,000 and most preferably about 6,000 to about 100,000. It may be polymerized from vinyl phosphonyl chloride by free radical polymerization in accordance with art recognized technique. The polyvinyl phosphonate is employed in amounts effective to inhibit enzymatic salivary hydrolysis of the linear molecularly dehydrated polyphosphate in amount up to about 4% by weight. It is generally employed in the compositions in approximate weight amounts of 0.05 to 4%, generally about 0.05 to 3%, preferably 0.05 to 2%, more preferably 0.1 to 2% by weight. Amounts of at least about 1% by weight are typically employed in dentifrice compositions, meaning oral compositions generally containing a dental abrasive and used in conjunction with brushing of the teeth, e.g. tooth pastes including gels and creams, and powders. Amounts in excess of 4% by weight may be employed for thickening or gelling purposes.

In addition to the polyvinyl phosphonate inhibitor of polyphosphate hydrolysis by the alkaline phosphatase salivary enzymes, additional hydrolysis inhibition is attained by the presence of a fluoride-ion source to inhibit hydrolysis by acid phosphatase and pyrophosphatase salivary enzymes. This material is preferably present and also serves to reduce caries formation.

The source of fluoride ions, or fluorine-providing compounds, which may be present as a combination enzyme inhibitor, are well known in the art as anti-caries agents and also act as such agents in the practice of this invention. 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 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 fluoride, barium fluoride, sodium fluosilicate, ammonium fluorosilicate, sodium fluorozirconate, sodium monofluorophosphate, aluminum mono-and di-fluorophosphate, and fluorinated sodium calcium pyrophosphate. Tin fluorides and particularly alkali metal fluorides, such as sodium fluoride and alkali metal monofluorophosphate (MFP), such as sodium MFP and mixtures thereof, are preferred.

The amount of fluorine-providing compound, when present, is dependent to some extent upon the type of compound, its solubility, and the type of oral preparation, but it must be a nontoxic amount. generally about 0.005 to about 3.0% in the preparation. In a dentifrice preparation, e.g. gel, cream, toothpaste or toothpowder, an amount of such compound which releases up to about 2,000 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 about 2,000 ppm. more preferably about 800 to about 1,500 ppm of fluoride ion. Typically, in the cases of alkali metal fluorides and stannous fluoride, 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 0.05% 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 oral preparations such as mouthwashes, lozenges and chewing gum, the fluorine-providing compound, when present, is 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 2:1 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 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.).

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 toothpaste (including gel or dental cream). The vehicle of such solid or pasty oral preparation generally contains a dentally acceptable water-insoluble polishing material. Examples of polishing materials are water-insoluble sodium metaphosphate, potassium metaphosphate, tricalcium phosphate, dihydrated dicalcium phosphate, anhydrous dicalcium phosphate, calcium pyrophosphate, magnesium orthophosphate, trimagnesium phosphate, calcium carbonate, aluminum silicate, zirconium silicate, siliceous polishing agent, bentonite, and mixtures thereof. Other suitable polishing materials 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 sizes 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, translucent or opacified gels are employed a siliceous polishing agent of colloidal silica, such as those sold under the trademark SYLOID as Syloid 72 and Syloid 74, Zeodent as Zeodent 113 and Zeodent 115 or under the trademark SANTOCEL as Santocel 100 and alkali metal alumino-silicate complexes or silica containing combined alumina, such as Zeo 49A or Zeo 49B, are particularly useful, since they have refractive indices close to the water and/or humectant) systems commonly used in dentifrices.

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 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 about 1% of the material is larger than about 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 90% by weight of the preparation. Glycerine, propylene glycol, sorbitol, polypropylene glycol and/or polyethylene glycol (e.g. 400-600) exemplify suitable humectant 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 80 wt.% of glycerine, and about 20-80 wt.% of sorbitol is preferably employed.

Toothpastes (including 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 5% by weight. 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.

Other suitable gelling agents include Irish moss, gum tragacanth, starch, polyvinylpyrrolidone, hydroxyethyl propylcellulose, hydroxybutyl methyl cellulose, hydroxypropyl methyl cellulose, hydroxyethyl cellulose (e.g. available as Natrosol), sodium carboxymethyl cellulose, xanthan and colloidal silica such as finely ground Syloid (e.g. 244). As mentioned earlier, the synthetic anionic polyvinyl phosphonate can also provide thickening or gelling properties. Colloidal silica such as finely ground Syloid (e.g. 244) is also a suitable thickener.

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 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 detersive material which imparts to the composition detersive 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 sulfoacetates higher fatty acid esters of 1,2 dihydroxy propane 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. sorbitan monostearate) and polypropyleneoxide (e.g. block copolymer Pluronic materials).

Various other materials may be incorporated in the oral preparations of this invention such as whitening agents, preservatives, silicones, chlorophyll compounds, other anticalculus agents, 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, which would complex with the active components of the instant invention are desirably 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, APM laspartyl phenyl alanine, methyl ester), saccharine and the like. Suitably, flavor and sweetening agents may together comprise from about 0.1% to 5% or 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 described polyphosphate and inhibitor combination in an amount effective to inhibit calculus on dental surfaces is preferably applied regularly to dental enamel, such as every second or third day or 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 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 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 and proportions referred to herein and in the appended claims are by weight and temperatures are in degrees C. unless otherwise indicated.

Example 1:

Inhibition of alkaline phosphatase by PVPA and PVMEMA

A reaction mixture is provided containing 0.05 units of E. Coli alkaline phosphatase in a total volume of 0.5 ml, with 100mM Tris-HCl buffer, pH of 8.0, in which a final concentration of 0.5mM tetrasodium pyrophosphate is present. The reaction is run at 37°C after the addition of pyrophosphate for varying amounts of time. The pH of polyvinyl phosphonate, mol. wt. 10,000(PVPA), or of polymeric polycarboxylate, polyvinyl methyl ether/maleic anhydride available from GAF Company as Gantrez S-97(PVME/MA) which has been reported to have a mol. wt. of about 70,000 (by vapor pressure osmometry; but which is determined to have a molecular weight of about 1,090,000 when determined by gel permeation chromatography) is pre-adjusted to 8.0 prior its being added to the reaction mixture in amount of 0.5%. The reaction is

terminated by adding 0.5 ml of 20% cold trichloroacetic (TCA). The amount of orthophosphate released is set forth in the Table 1 below and is calculated as follows:

For each mole of pyrophosphate ion (PPi) hydrolyzed, two moles of orthophosphates are released according to the equation: On a weight basis, the amount of

$$\text{PPi hydrolyzed (g)} = \frac{\text{Molecular Weight } P_2O_7}{2X(\text{Molecular Weight } PO_4)} \text{ X amount of } PO_4 \text{ generated (g)}$$

TABLE 1

Mean Pyrophosphate Hydrolyzed (ug/ml)			
Reaction Time (min.)	Control Without Inhibitor	+ PVME/MA	+ PVPA
4.0	20.53	7.94	4.62
8.0	27.04	7.92	5.28

The data show that PVPA inhibits alkaline phosphatase to a greater extent than does PVME/MA.

Example 2:

Anticalculus Effect In Vivo

Water and the indicated solutions are tested in a rat calculus study with the results shown in Table 2 below:

TABLE 2

Mean Calculus Surface		
Treatment	Severity Index ± Standard Deviation	% Change
A. Water	61.8 (± 10.4)	
B. 6.2% $K_4P_2O_7$, 1% PVPA + 0.24% NaF	27.8 (± 8.6)	-55%

It is clear that Treatment B is highly effective against calculus formation in vivo.

The rat calculus study is conducted as follows:

Twenty-one day old male weanling Sprague-Dawley rats are randomized among the treatment groups containing 12 rats per group. The animals are fed calculogenic diet (RC-16) and deionized water, ad libitum, during the entire study. Before initiation of the experimental treatments all animals are inoculated with a suspension of S. mutans (6715) and A. viscosus (OMZ-105-NYL) to stimulate plague and calculus formation. The rats are treated once daily (excluding weekends) with 0.2 ml of solution using an automatic pipettor.

The experiment is conducted blind; the treatments are coded and unknown to the personnel involved. Rats are sacrificed after 21 days of treatment and the jaws prepared for scoring according to routine methods (SPI TOX 626). Body weights are taken initially and at the time of sacrifice. Calculus on both the maxillary and mandibular guadrants of each rat are evaluated using the method of Briner and Francis reported in "Calcified Tissue Research", Vol. 11, Pages 10-22, 1973, which describes the Calculus Surface Severity Index (CSSI). Statistical analysis of the data are performed using ANOVA plus the Student-Newman-Keuls Test.

EXAMPLE 3

The following toothpastes are prepared:

	Parts			
	A	B	C	D
Water (Deionized)	42.42	27.46	26.14	20.12
Glycerine	25.00	10.00	10.00	25.00
Sorbitol (70%)	-	25.00	25.00	-
Polyethylene Glycol 600	-	3.00	3.00	-
Tetrasodium Pyrophosphate	2.0	1.50	-	-
Tetrapotassium Pyrophosphate	-	4.50	-	-
Sodium Tripolyphosphate	-	-	6.00	-
Sodium Hexametaphosphate	-	-	-	6.00
Xanthan	1.00	-	-	1.00
Sodium Carboxyethyl Cellulose	-	1.20	1.20	-
Silica Thickener (Syloid 244)	3.00	-	-	3.00
PVPA	0.50	0.50	1.00	0.50
Sodium Monofluorophosphate	0.76	-	0.76	0.76
Sodium Fluoride	-	0.24	-	-
Silica containing combined Alumina (Zeo 49B)	21.50	-	-	-
Colloidal Silica (Zeodent 113)	-	23.00	23.00	-
Calcium Pyrophosphate	-	-	-	40.00
Sodium Benzoate	0.50	0.50	0.50	0.50
Titanium Dioxide	0.50	0.30	0.30	0.30
Sodium Saccharine	0.30	0.30	0.30	0.30
Flavor	1.00	1.00	1.00	1.00
Sodium Lauryl Sulfate	1.20	1.20	1.20	1.20
Sodium Hydroxide (50%)	0.32	0.30	0.60	0.32

EXAMPLE 4

The following mouthwashes are prepared:

	Parts	
	A	B
Ethyl Alcohol	10.00	10.00
Glycerine	10.00	10.00
Sodium Saccharine	0.03	0.03
Block Copolymer Pluronic F 108	2.00	2.00
Tetrasodium Pyrophosphate	2.00	1.00
Tetrapotassium Pyrophosphate	-	1.00
Disodium Pyrophosphate	-	0.10
PVPA	0.05	0.05
Sodium Monofluorophosphate	0.15	0.15
Flavor	0.40	0.40
Water	Q.S. to 100.00	Q.S. to 100.00

Example 5

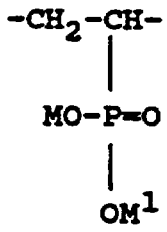
Lozenges	
Sugar	78-98
Corn syrup	1-20
Flavor oil	0.1-1.0
Tablet lubricant	0.1-5
Polyphosphate	0.1-5
PVPA	0.05-3
NaF	0.01-0.05
Water	0.01-0.2

Example 6

Chewing Gum	
Gum base	10 to 50
Binder	3 to 10
Filler (sorbitol, mannitol or combination thereof)	5 to 80
Artificial sweetener	0.1 to 5
Polyphosphate	0.1 to 5
PVPA	0.1 to 1.0
NaF	0.01-0.05
Flavor	0.1 to 5

The 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.

According to broader aspects of the present invention an anticalculus oral composition, which is believed to inhibit the transformation of amorphous calcium phosphate to HAP crystal structure normally associated with calculus, comprises, in an orally acceptable vehicle an effective anticalculus amount of at least one linear molecularly dehydrated polyphosphate salt as essential anticalculus agent, and, an effective amount of an inhibitor against enzymatic hydrolysis of the said agent in saliva, characterised in that the inhibitor comprises a synthetic anionic polyvinyl phosphonate, having recurring groups of the formula:



and an average molecular weight of at least about 1,000 and greater; and wherein M and M^1 represent a hydrogen atom or an alkali metal or ammonium group, and wherein M and M^1 are the same or different.

The said polyvinyl phosphonate is preferably present in amount of up to about 4% e.g. about 0.05-4% by weight, more preferably about 0.05-3% by weight, especially about 0.1-2% by weight. The said polyvinyl phosphonate preferably has a molecular weight of about 1,000 to about 1,000,000, more preferably about 6,000 to about 100,000.

The said polyphosphate salt is preferably present in amount of about 0.1-7% by weight.

The said polyphosphate salt is preferably selected from the group consisting of hexametaphosphates, tripolyphosphates, pyrophosphates and mixtures thereof, especially tetrasodium pyrophosphate, and tetrapotassium pyrophosphate and mixtures thereof.

The said polyphosphate salt is preferably present in amount of about 4.3-7% by weight and is a mixture of tetrapotassium pyrophosphate and tetrasodium pyrophosphate, with the amount of tetrapotassium pyrophosphate being predominant over the amount of tetrasodium pyrophosphate.

In other forms of the invention the polyphosphate salt may be tetrasodium pyrophosphate e.g. present in amount of about 0.1-2% by weight, or the said polyphosphate salt may be a tripolyphosphate, or may be a hexametaphosphate.

In one preferred form of the invention, the said vehicle comprises about 10% - 90% by weight of a liquid vehicle comprising water and humectant and about 0.1-10% by weight of a gelling agent and there is present about 10-75% by weight of a dentally acceptable water-insoluble polishing agent; the said oral composition being a toothpaste.

The polishing agent may be a siliceous polishing agent.

In another preferred form of the invention the said vehicle is about 70-99.9% by weight of a water-alcohol mixture, the weight ratio of water to alcohol being from about 1:1 to about 20:1; the said oral composition being a mouthwash.

Compositions in accordance with the invention desirably include a fluoride-ion source present in amount sufficient to supply a non-toxic amount of about 25-2,000 ppm of fluoride ions, as an anticaries agent and as a further inhibitor against enzymatic hydrolysis of the said essential anticalculus agent.

The fluoride-ion source is preferably selected from the group consisting of alkali metal fluoride, e.g. sodium fluoride, and alkali metal monofluorophosphate.

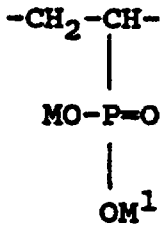
The invention also extends to a method of inhibiting dental calculus comprising applying to teeth a calculus-inhibiting amount of an oral composition in accordance with the invention, the said oral composition having a pH of about 4.5 to about 9.

Claims

1. An anticalculus oral composition comprising, in an orally acceptable vehicle an effective anticalculus amount of at least one linear molecularly dehydrated water soluble polyphosphate salt as essential anticalculus agent, and, an effective amount of an inhibitor against enzymatic hydrolysis of the said agent in saliva, characterised in that the

The 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.

According to broader aspects of the present invention an anticalculus oral composition, which is believed to inhibit the transformation of amorphous calcium phosphate to HAP crystal structure normally associated with calculus, comprises, in an orally acceptable vehicle an effective anticalculus amount of at least one linear molecularly dehydrated polyphosphate salt as essential anticalculus agent, and, an effective amount of an inhibitor against enzymatic hydrolysis of the said agent in saliva, characterised in that the inhibitor comprises a synthetic anionic polyvinyl phosphonate, having recurring groups of the formula:



and an average molecular weight of at least about 1,000 and greater; and wherein M and M^1 represent a hydrogen atom or an alkali metal or ammonium group, and wherein M and M^1 are the same or different.

The said polyvinyl phosphonate is preferably present in amount of up to about 4% e.g. about 0.05-4% by weight, more preferably about 0.05-3% by weight, especially about 0.1-2% by weight. The said polyvinyl phosphonate preferably has a molecular weight of about 1,000 to about 1,000,000, more preferably about 6,000 to about 100,000.

The said polyphosphate salt is preferably present in amount of about 0.1-7% by weight.

The said polyphosphate salt is preferably selected from the group consisting of hexametaphosphates, tripolyphosphates, pyrophosphates and mixtures thereof, especially tetrasodium pyrophosphate, and tetrapotassium pyrophosphate and mixtures thereof.

The said polyphosphate salt is preferably present in amount of about 4.3-7% by weight and is a mixture of tetrapotassium pyrophosphate and tetrasodium pyrophosphate, with the amount of tetrapotassium pyrophosphate being predominant over the amount of tetrasodium pyrophosphate.

In other forms of the invention the polyphosphate salt may be tetrasodium pyrophosphate e.g. present in amount of about 0.1-2% by weight, or the said polyphosphate salt may be a tripolyphosphate, or may be a hexametaphosphate.

In one preferred form of the invention, the said vehicle comprises about 10% - 90% by weight of a liquid vehicle comprising water and humectant and about 0.1-10% by weight of a gelling agent and there is present about 10-75% by weight of a dentally acceptable water-insoluble polishing agent; the said oral composition being a toothpaste.

The polishing agent may be a siliceous polishing agent.

In another preferred form of the invention the said vehicle is about 70-99.9% by weight of a water-alcohol mixture, the weight ratio of water to alcohol being from about 1:1 to about 20:1; the said oral composition being a mouthwash.

Compositions in accordance with the invention desirably include a fluoride-ion source present in amount sufficient to supply a non-toxic amount of about 25-2,000 ppm of fluoride ions, as an anticaries agent and as a further inhibitor against enzymatic hydrolysis of the said essential anticalculus agent.

The fluoride-ion source is preferably selected from the group consisting of alkali metal fluoride, e.g. sodium fluoride, and alkali metal monofluorophosphate.

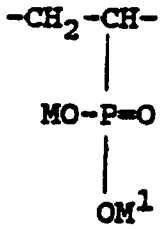
The invention also extends to a method of inhibiting dental calculus comprising applying to teeth a calculus-inhibiting amount of an oral composition in accordance with the invention, the said oral composition having a pH of about 4.5 to about 9.

Claims

1. An anticalculus oral composition comprising, in an orally acceptable vehicle an effective anticalculus amount of at least one linear molecularly dehydrated water soluble polyphosphate salt as essential anticalculus agent, and, an effective amount of an inhibitor against enzymatic hydrolysis of the said agent in saliva, characterised in that the

* C L M S *

inhibitor comprises a synthetic anionic polyvinyl phosphonate, having recurring groups of the formula:



and an average molecular weight of at least about 1,000 and greater; and wherein M and M^1 represent a hydrogen atom or an alkali metal or ammonium group, and wherein M and M^1 are the same or different.

2. An oral composition as claimed in Claim 1 characterised in that the said polyvinyl phosphonate is present in amount of up to 4% by weight.

3. An oral composition as claimed in Claim 2 characterised in that the said polyvinyl phosphonate is present in amount of about 0.05-4% by weight.

4. An oral composition as claimed in Claim 1, 2 or 3 characterised in that the said polyvinyl phosphonate has a molecular weight of about 1,000 to about 1,000,000.

5. An oral composition as claimed in any one of Claims 1 to 4 characterised in that the said polyphosphate salt is present in amount of about 0.1-7% by weight.

6. An oral composition as claimed in any one of Claims 1 to 5 characterised in that the said polyphosphate salt is selected from the group consisting of hexametaphosphates, tripolyphosphates, pyrophosphates and mixtures thereof.

7. An oral composition claimed in Claim 6 characterised in that the said polyphosphate salt is selected from the group consisting of tetrasodium pyrophosphate, tetrapotassium pyrophosphate and mixtures thereof.

8. An oral composition as claimed in any one of Claims 1 to 7 characterised in that the said polyphosphate salt is present in amount of about 4.3-7% by weight and is a mixture of tetrapotassium pyrophosphate and tetrasodium pyrophosphate, with the amount of tetrapotassium pyrophosphate being predominant over the amount of tetrasodium pyrophosphate.

9. An oral preparation as claimed in any one of Claims 1 to 8 characterised in that the said polyphosphate salt is tetrasodium pyrophosphate which is present in amount of about 0.1-2% by weight.

10. An oral composition as claimed in any one of Claims 1 to 9 characterised in that the said vehicle comprises about 10% - 90% by weight of a liquid vehicle comprising water and humectant and about 0.1-10% by weight of a gelling agent and wherein there is present about 10-75% by weight of a dentally acceptable water-insoluble polishing agent; the said oral composition being a toothpaste.

11. An oral composition as claimed in any one of Claims 1 to 9 characterised in that the said vehicle is about 70-99.9% by weight of a water-alcohol mixture, the weight ratio of water to alcohol being from about 1:1 to about 20:1; the said oral composition being a mouthwash.

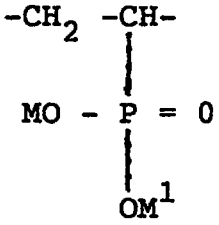
12. An oral composition as claimed in any one of Claims 1 to 11 characterised in that a fluoride-ion source is present in amount sufficient to supply a non-toxic amount of about 25-2,000 ppm of fluoride ions, as an anticaries agent and as a further inhibitor against enzymatic hydrolysis of the said essential anticalculus agent.

Patentansprüche

1. Oral anwendbare, zahnsteinverhindernde Zusammensetzung, die in einem oral akzeptablen Träger eine wirksam zahnsteinverhindernde Menge mindestens eines linearen, molekular dehydratisierten, in Wasser löslichen Polyphosphatsalzes als essentielles zahnsteinverhinderndes Mittel und eine wirksame Menge eines Inhibitors gegen

* C L M S *

enzymatische Hydrolyse dieses Mittels im Speichel umfaßt, dadurch gekennzeichnet, daß der Inhibitor ein synthetisches anionisches Polyvinylphosphonat umfaßt, das wiederkehrende Gruppen der Formel:



und ein durchschnittliches Molekulargewicht von mindestens etwa 1 000 und größer aufweist, wobei M und M^1 für ein Wasserstoffatom oder ein Alkalimetallatom oder eine Ammoniumgruppe stehen und M und M^1 gleich oder verschieden sind.

2. Oral anwendbare Zusammensetzung nach Anspruch 1, dadurch gekennzeichnet, daß das Polyvinylphosphonat in einer Menge von bis zu 4 Gew.% vorhanden ist.

3. Oral anwendbare Zusammensetzung nach Anspruch 2, dadurch gekennzeichnet, daß das Polyvinylphosphonat in einer Menge von etwa 0,05 bis 4 Gew.% vorhanden ist.

4. Oral anwendbare Zusammensetzung nach Anspruch 1, 2 oder 3, dadurch gekennzeichnet, daß das Polyvinylphosphonat ein Molekulargewicht von etwa 1 000 bis etwa 1 000 000 aufweist.

5. Oral anwendbare Zusammensetzung nach einem der Ansprüche 1 bis 4, dadurch gekennzeichnet, daß das Polyphosphatsalz in einer Menge von etwa 0,1 bis 7 Gew.% vorhanden ist.

6. Oral anwendbare Zusammensetzung nach einem der Ansprüche 1 bis 5, dadurch gekennzeichnet, daß das Polyphosphatsalz ausgewählt ist aus der Gruppe bestehend aus Hexametaphosphaten, Tripolyphosphaten, Pyrophosphaten und Mischungen derselben.

7. Oral anwendbare Zusammensetzung nach Anspruch 6, dadurch gekennzeichnet, daß das Polyphosphatsalz ausgewählt ist aus der Gruppe bestehend aus Tetranatriumpyrophosphat, Tetrakaliumpyrophosphat und Mischungen derselben.

8. Oral anwendbare Zusammensetzung nach einem der Ansprüche 1 bis 7, dadurch gekennzeichnet, daß das Polyphosphatsalz in einer Menge von etwa 4,3 bis 7 Gew.% vorhanden ist und eine Mischung aus Tetrakaliumpyrophosphat und Tetranatriumpyrophosphat ist, wobei die Menge an Tetrakaliumpyrophosphat gegenüber der Menge an Tetranatriumpyrophosphat überwiegt.

9. Oral anwendbare Zusammensetzung nach einem der Ansprüche 1 bis 8, dadurch gekennzeichnet, daß das Polyphosphatsalz Tetranatriumpyrophosphat ist, das in einer Menge von etwa 0,1 bis 2 Gew.% vorhanden ist.

10. Oral anwendbare Zusammensetzung nach einem der Ansprüche 1 bis 9, dadurch gekennzeichnet, daß der Träger etwa 10 bis 90 Gew.% eines flüssigen Trägers, der Wasser und Feuchthaltemittel umfaßt, und etwa 0,1 bis 10 Gew.% Gelierungsmittel umfaßt, wobei etwa 10 bis 75 Gew.% eines dental akzeptablen, in Wasser unlöslichen Poliermittels vorhanden sind und die oral anwendbare Zusammensetzung eine Zahnpasta ist.

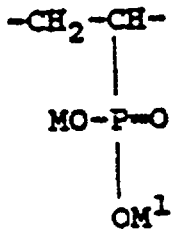
11. Oral anwendbare Zusammensetzung nach einem der Ansprüche 1 bis 9, dadurch gekennzeichnet, daß der Träger aus etwa 70 bis 99,9 Gew.% einer Wasser/Alkohol-Mischung besteht, wobei das Gewichtsverhältnis von Wasser zu Alkohol etwa 1:1 bis etwa 20:1 beträgt und die oral anwendbare Zusammensetzung ein Mundspülmittel ist.

12. Oral anwendbare Zusammensetzung nach einem der Ansprüche 1 bis 11, dadurch gekennzeichnet, daß eine Fluoridionenquelle in einer Menge, die ausreicht, um eine nicht-toxische Menge von etwa 25 bis 2 000 ppm Fluoridionen zu liefern, als ein Antikariesmittel und ferner als ein Inhibitor gegen enzymatische Hydrolyse des essenziellen zahnsteinverhindernden Mittels vorhanden ist.

* C L M S *

Revendications

1. Composition buccale anti-tartre comprenant dans un véhicule acceptable pour une administration par voie orale, une quantité efficace du point de vue du détartrage d'au moins un sel polyphosphate hydrosoluble déshydraté au niveau moléculaire en tant qu'agent anti-tartre essentiel, et une quantité efficace d'un inhibiteur de l'hydrolyse enzymatique dudit agent dans la salive, caractérisée en ce que l'inhibiteur comprend un polyvinylphosphonate anionique synthétique, présentant des motifs récurrents de formule :



et un poids moléculaire moyen au moins d'environ 1 000 ou plus ; et dans laquelle M et M^1 représentent un atome d'hydrogène ou un métal alcalin ou un groupe ammonium, et dans laquelle M et M^1 sont identiques ou différents.

2. Composition buccale selon la revendication 1, caractérisée en ce que ledit polyvinylphosphonate est présent à raison de jusqu'à 4 % en poids.

3. Composition buccale selon la revendication 2, caractérisée en ce que ledit polyvinylphosphonate est présent à raison d'environ 0,05-4 % en poids.

4. Composition buccale selon la revendication 1, 2 ou 3, caractérisée en ce que ledit polyvinylphosphonate a un poids moléculaire d'environ 1 000 à environ 1 000 000.

5. Composition buccale selon l'une quelconque des revendications 1 à 4, caractérisée en ce que ledit sel polyphosphate est présent à raison d'environ 0,1-7 % en poids.

6. Composition buccale selon l'une quelconque des revendications 1 à 5, caractérisée en ce que ledit sel polyphosphate est choisi parmi le groupe constitué de hexamétaphosphates, tripolyphosphates, pyrophosphates et leurs mélanges.

7. Composition buccale selon la revendication 6, caractérisée en ce que ledit sel polyphosphate est choisi dans le groupe constitué de pyrophosphate tétrasodique, pyrophosphate tétrapotassique et leurs mélanges.

8. Composition buccale selon l'une quelconque des revendications 1 à 7, caractérisée en ce que ledit sel polyphosphate est présent à raison d'environ 4,3-7 % en poids et est un mélange de pyrophosphate tétrapotassique et pyrophosphate tétrasodique, le pyrophosphate tétrapotassique étant majoritaire par rapport au pyrophosphate tétrasodique.

9. Composition buccale selon l'une quelconque des revendications 1 à 8, caractérisée en ce que ledit sel de polyphosphate est le pyrophosphate tétrasodique présent à raison d'environ 0,1-2 % en poids.

10. Composition buccale selon l'une quelconque des revendications 1 à 9, caractérisée en ce que ledit véhicule comprend environ 10-90 % en poids d'un véhicule liquide comprenant de l'eau et un agent humidifiant et environ 0,1 à 10 % en poids d'un agent gélifiant, un agent de polissage insoluble dans l'eau acceptable du point de vue dentaire étant présent à raison de 10-75 % en poids, ladite composition étant un dentifrice.

11. Composition buccale selon l'une quelconque des revendications 1 à 9, caractérisée en ce que ledit véhicule représente environ 70-99,9 % en poids d'un mélange d'alcool et d'eau, le rapport pondéral de l'eau à l'alcool étant d'environ 1:1 à environ 20:1 ; ladite composition buccale étant une composition buccale de rinçage.

12. Composition buccale selon l'une quelconque des revendications 1 à 11, caractérisée en ce que la source d'ion fluorure est présente en une quantité suffisante de façon à fournir une quantité non toxique d'environ 25-2 000 ppm

* C L M S *

d'ions fluorure, en tant qu'agent contre les caries et en tant qu'inhibiteur supplémentaire de l'hydrolyse enzymatique dudit agent anti-tartre essentiel.

* C L M S *