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Antiplaque antibacterial oral composition

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ANTIPLAQUE ANTIBACTERIAL ORAL COMPOSITION

This invention relates to antibacterial antiplaque oral compositions such as dentifrices and mouthwashes. More particularly, it relates to oral compositions containing a substantially water-insoluble noncationic antibacterial agent effective to inhibit plaque.

Dental plaque is a soft deposit which forms on teeth as opposed to calculus which is a hard calcified deposit on teeth. Unlike calculus, plaque may form on any part of the tooth surface, particularly including at the gingival margin. Hence, beside being unsightly, it is implicated in the occurence of gingivitis.

Accordingly, it is highly desirable to include antimicrobial agents which have been known to reduce plaque in oral compositions. Frequently, cationic antibacterial agents have been suggested. Moreover, in U.S. Patent 4,022,880 to Vinson et al, 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. The noncationic antibacterial antiplaque halogenated hydroxydiphenyl ether, triclosan, has also been described in combination with zinc citrate trihydrate in European Patent Publication 0161,899

to Saxton et al. Triclosan is also disclosed in European Patent Publication 0271,332 to Davis as a toothpaste component containing a solubilizing agent such as propylene glycol.

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, they are generally not effective when used with anionic materials. Noncationic antibacterial materials, on the other hand, can be compatible with anionic components in an oral composition.

However, oral compositions typically are mixtures of numerous components and even such typically neutral materials as humectants can affect performance of such compositions.

Moreover, even noncationic antibacterial agents may have limited antiplaque effectiveness with commonly used materials such as polyphosphate anticalculus agents which are disclosed together in British Patent Publication 22 00551 of Gaffar et al and in EP 0251591 of Jackson et al.

It is an advantage of this invention that an oral composition is provided wherein a substantially water-insoluble noncationic antibacterial agent and an AEA is provided to inhibit plaque formation, wherein the oral composition contains an orally acceptable liquid vehicle effective to enable said antibacterial agent to dissolve in saliva in effective antiplaque amount.

It is a further advantage of this invention that the AEA enhances the delivery and retention of small but effective antiplaque amount of the antibacterial agent on teeth and on soft oral tissues.

It is a further advantage of this invention that an antiplaque oral composition is provided which is effective to reduce the occurrence of gingivitis.

Additional advantages of this invention will be apparent from consideration of the following specification.

In accordance with this invention an oral composition comprises an effective antiplaque amount of a substantially water insoluble noncationic antibacterial agent, and an antibacterial-enhancing agent

which has an average molecular weight of 1,000 to 1,000,000, and contains at least one delivery enhancing functional group and at least one organic retention enhancing group, the said agent containing the said groups being free from or substantially free from water soluble alkali metal or ammonium synthetic anionic linear polymer polycarboxylate salt having a molecular weight of about 1,000 to about 1,000,000, the said oral composition being free of polyphosphate anticalculus agent.

The composition preferably comprises 0.005-4% by weight of the antibacterial enhancing agent.

~~the said oral composition being free of polyphosphate anticalculus agent.~~

Typical examples of water insoluble noncationic antibacterial agents which are particularly desirable from considerations of antiplaque effectiveness, safety and formulation are:

Halogenated Diphenyl Ethers

2',4,4'-trichloro-2-hydroxy-diphenyl ether (Triclosan)

2,2'-dihydroxy-5,5'-dibromo-diphenyl ether.

Halogenated Salicylanilides

4',5-dibromosalicylanilide

3,4',5-trichlorosalcylanilide

3,4',5-tribromosalicylanilide

2,3,3',5-tetrachlorosalicylanilide

3,3,3',5-tetrachlorosalicylanilide

3,5-dibromo-3'-trifluoromethyl salicylanilide

5-n-octanoyl-3'-trifluoromethyl salicylanilide

3,5-dibromo-4'-trifluoromethyl salicylanilide

3,5-dibromo-3'-trifluoro methyl salicylanilide (Flurophene)

Benzoic Esters

Methyl - p-Hydroxybenzoic Ester

Ethyl - p-Hydroxybenzoic Ester

Propyl - p-Hydroxybenzoic Ester

Butyl - p-Hydroxybenzoic Ester

Halogenated Carbanilides

3,4,4'-trichlorocarbanilide

3-trifluoromethyl-4,4'-dichlorocarbanilide

3,3,4'-trichlorocarbanilide

Phenolic Compounds (including phenol and its homologs, mono- and poly-alkyl and aromatic halo (e.g. F, Cl, Br, I.)-phenols, resorcinol and catechol and their derivatives and bisphenolic compounds)

Phenol and its Homologs

Phenol

2 Methyl - Phenol

3 Methyl - Phenol

4 Methyl - Phenol

4 Ethyl - Phenol

2,4-Dimethyl - Phenol

2,5-Dimethyl - Phenol

3,4-Dimethyl - Phenol

2,6-Dimethyl - Phenol

4-n Propyl - Phenol

4-n-Butyl - Phenol

4-n-Amyl - Phenol

4-tert-Amyl - Phenol

4-n-Hexyl - Phenol

4-n-Heptyl - Phenol

2-Methoxy-4-(2-Propenyl)-Phenol (Eugenol)

2-Isopropyl-5-Methyl - Phenol (Thymol)

Mono- and Poly-Alkyl and Aralkyl Halophenols

Methyl - p-Chlorophenol

Ethyl - p-Chlorphenol

n-Propyl - p-Chlorophenol

n-Butyl - p-Chlorophenol

n-Amyl - p-Chlorophenol

sec-Amyl - p-Chlorophenol

n-Hexyl - p-Chlorophenol

cyclohexyl - p-Chlorophenol

n-Heptyl - p-Chlorophenol

n-Octyl - p-Chlorophenol

O-Chlorophenol

Methyl - o-Chlorophenol

Ethyl - o-Chlorophenol

n-Propyl - o-Chlorophenol

n-Butyl - o-Chlorophenol

n-Amyl - o-Chlorophenol

tert-Amyl - o-Chlorophenol

n-Hexyl - o-chlorophenol

n-Heptyl - o-Chloropenol

p-Chlorophenol

o-Benzyl - p-Chlorophenol

o-Benzyl-m-methyl - p-Chlorophenol

o-Benzyl-m, m-dimethyl - p-Chlorophenol

o-Phenylethyl - p-Chlorophenol

o-Phenylethyl-m-methyl - p-Chlorophenol

3-Methyl - p-Chlorophenol

3,5-Dimethyl - p-Chlorophenol

6-Ethyl-3-methyl - p-Chlorophenol

6-n-Propyl-3-methyl - p-Chlorophenol

6-iso-propyl-3-methyl - p-Chlorophenol

2-Ethyl-3,5-dimethyl - p-Chlorophenol

6-sec Butyl-3-methyl - p-Chlorophenol

2-iso-Propyl-3,5-dimethyl - p-Chlorophenol

6-Diethylmethyl-3-methyl - p-Chlorophenol

6-iso-Propyl-2-ethyl-3-methyl - p-Chlorophenol

2-sec Amyl-3,5-dimethyl - p-Chlorophenol

2-Diethylmethyl-3,5-dimethyl - p-Chlorophenol

6-sec Octyl-3-methyl - p-Chlorophenol

p-Bromophenol

Methyl - p-Bromophenol

Ethyl - p-Bromophenol

n-Propyl - p-Bromophenol

n-Butyl - p-Bromophenol

n-Amyl - p-Bromophenol

sec-Amyl - p-Bromophenol

n-Hexyl - p-Bromophenol

cyclohexyl - p-Bromophenol

o-Bromophenol

tert-Amyl - o-Bromophenol

n-Hexyl - o-Bromophenol

n-Propyl-m,m-Dimethyl - o-Bromophenol

2-Phenyl Phenol

4-Chloro-2-methyl phenol

4-chloro-3-methyl phenol

4-chloro-3,5-dimethyl phenol

2,4-dichloro-3,5-dimethyl phenol

3,4,5,6-tetrabromo-2-methylphenol

5-methyl-2-pentylphenol

4-isopropyl-3-methylphenol

5-chloro-2-hydroxydiphenyl methane

Resorcinol and Its Derivatives

Resorcinol

Methyl - Resorcinol

Ethyl - Resorcinol

n-Propyl - Resorcinol

n-Butyl - Resorcinol

n-Amyl - Resorcinol

n-Hexyl - Resorcinol

n-Heptyl - Resorcinol

n-Octyl - Resorcinol

n-Nonyl - Resorcinol

Phenyl - Resorcinol

Benzyl - Resorcinol

Phenylethyl - Resorcinol

Phenylpropyl - Resorcinol

p-Chlorobenzyl - Resorcinol

5-Chloro -2,4-Dihydroxydiphenyl Methane

4'-Chloro -2,4-Dihydroxydiphenyl Methane

5-Bromo -2,4-Dihydroxydiphenyl Methane

4"-Bromo -2,4-Dihydroxydiphenyl Methane

Bisphenolic Compounds

Bisphenol A

2,2'-methylene bis (4-chlorophenol)

2,2'-methylene bis (3,4,6-trichlorophenol) (hexachlorophene)

2,2'-methylene bis (4-chloro-6-bromophenol)

bis (2-hydroxy-3,5-dichlorophenyl) sulfide

bis (2-hydroxy-5-chlorobenzyl) sulfide

The noncationic antibacterial agent is present in the oral composition in an effective antiplaque amount preferably about 0.01%-5% by weight, more preferably about 0.03%-1%, more preferably about 0.25-0.5% or about 0.25% to less than 0.5% and most preferably about 0.25-0.35%, e.g. about 0.3%, in a dentifrice or preferably about 0.03-0.3% by weight, most preferably about 0.03-0.1% in a mouthwash or liquid dentifrice. The antibacterial agent 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%.

The preferred halogenated diphenyl ether is triclosan. The preferred phenolic compounds are phenol, thymol, eugenol, hexyl resorcinol and 2,2'methylene bis (4-chloro-6-bromophenol). The most preferred antibacterial antiplaque compound is triclosan. Triclosan is disclosed in aforementioned U.S. Patent 4,022,880 as an antibacterial agent in combination with an anticalculus agent which provides zinc ions and in German Patent Disclosure 3532860

in combination with a copper compound. In European Patent Disclosure 0278744 it is disclosed in combination with a tooth desensitizing agent containing a source of potassium ions. It is also disclosed as an antiplaque agent in a dentifrice formulated to contain a lamellar liquid crystal surfactant phase having a lamellar spacing of less than 6.0 nm and which may optionally contain a zinc salt in published European Patent Application 0161898 of Lane et al and in a dentifrice containing zinc citrate trihydrate in published European Patent Application 0161899 to Saxton et al.

The antibacterial-enhancing agent (AEA) which enhances delivery of said antibacterial agent to, and retention thereof on, oral surfaces, is employed in amounts effective to achieve such enhancement preferably within the range in the oral composition of about 0.005% to about 4%, preferably about 0.1% to about 3%, more preferably about 0.5% to about 2.5% by weight.

The AEA may be a simple compound, preferably a polymerizable monomer, more preferably a polymer, which latter term is entirely generic, including for example oligomers, homopolymers, copolymers of two or more monomers, ionomers, block copolymers, graft copolymers, cross-linked polymers and copolymers, and the like. The AEA may be natural or synthetic, and water insoluble or preferably water (saliva) soluble or swellable (hydratable, hydrogel forming). It has an (weight) average molecular weight

of 1,000 to 1,000,000, more preferably about 2,000 or 2,500 to about 250,000 or 500,000.

The AEA contains at least one delivery-enhancing group, which is preferably acidic such as sulfonic, phosphonic, or more preferably phosphonic, or salt thereof, e.g. alkali metal or ammonium, and at least one organic retention-enhancing group, preferably a plurality of both the delivery-enhancing and retention-enhancing groups, which latter groups preferably have the formula $-(X)_n-R$ wherein X is O, N, S, SO, SO_2, P, PO or Si or the like, R is hydrophobic alkyl, alkenyl, acyl, aryl, alkaryl, aralkyl, heterocyclic or their inert-substituted derivatives, and n is zero or 1. The aforesaid "inert-substituted derivatives", are intended to include substituents on R which are generally non-hydrophilic and do not significantly interfere with the desired functions of the AEA as enhancing the delivery of the antibacterial agent to, and retention thereof on, oral surfaces such as halo, e.g. Cl, Br, I, and carbo and the like. Illustrations of such retention-enhancing groups are tabulated below.

n	X	$-(X)_nR$
0	---	methyl, ethyl, propyl, butyl, isobutyl, t-butyl cyclohexyl, allyl, benzyl, phenyl, chlorophenyl, xylyl, pyridyl, furanyl, acetyl, benzoyl, butyryl, terephthaloyl, etc.
1	O	ethoxy, benzyloxy, thioacetoxy, phenoxy, carboethoxy, carbobenzyloxy, etc.
	N	ethylamino, diethylamino, propylamido, benzylamino, benzoylamido, phenylacetamido, etc.
	S	thiobutyl, thioisobutyl, thioallyl, thiobenzyl, thiophenyl, thiopropionyl, phenylthioacetyl, thiobenzoyl, etc.
	SO	butylsulfoxy, allylsulfoxy, benzylsulfoxy, phenylsulfoxy, etc.
	SO_2	butylsulfonyl, allylsulfonyl, benzylsulfonyl, phenylsulfonyl, etc.
	P	diethylphosphinyl, ethylvinylphosphinyl, ethylallylphosphinyl, ethylbenzylphosphinyl, ethylphenylphosphinyl, etc.
	PO	diethylphosphinoxy, ethylvinylphosphinoxy, methylallylphosphinoxy, methylbenzylphosphinoxy, methylphenylphosphinoxy, etc.
	Si	trimethylsilyl, dimethylbutylsilyl, dimethylbenzylsilyl, dimethylvinylsilyl, dimethylallylsilyl, etc.

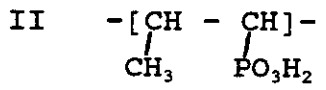
As employed herein, the delivery-enhancing group refers to one which attaches or substantively, adhesively, cohesively or otherwise bonds the AEA (carrying the antibacterial agent) to oral (e.g. tooth and gum) surfaces, thereby "delivering" the antibacterial agent to such surfaces. The organic retention-enhancing group, generally

hydrophobic, attaches or otherwise bonds the antibacterial agent to the AEA, thereby promoting retention of the antibacterial agent to the AEA and indirectly on the oral surfaces. In some instances, attachment of the antibacterial agent occurs through physical entrapment thereof by the AEA, especially when the AEA is a cross-linked polymer, the structure of which inherently provides increased sites for such entrapment. The presence of a higher molecular weight, more hydrophobic cross-linking moiety in the cross-linked polymer still further promotes the physical entrapment of the antibacterial agent to or by the cross-linked AEA polymer.

Preferably, the AEA is a anionic polymer comprising a chain or backbone containing repeating units each preferably containing at least one carbon atom and at least one directly or indirectly pendent, monovalent delivery-enhancing group and at least one directly or indirectly pendent monovalent retention-enhancing group geminally, vicinally or less preferably otherwise bonded to atoms, preferably carbon, in the chain. Less preferably, the polymer may contain delivery-enhancing groups and/or retention-enhancing groups and/or other divalent atoms or groups as links in the polymer chain instead of or in addition to carbon atoms, or as cross-linking moieties.

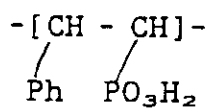
In the case of the preferred polymeric AEA's, it is desirable, for maximizing substantivity and delivery of the antibacterial agent to oral surfaces, that the repeating units in the polymer chain or backbone containing the acidic delivery enhancing groups constitute at least about 10%, preferably at least about 50%, more preferably at least about 80% up to 95% or 100% by weight of the polymer.

According to a preferred embodiment of this invention, the AEA comprises a polymer containing repeating units in which one or more phosphonic acid delivery-enhancing groups are bonded to one or more carbon atoms in the polymer chain, which contains a retention-enhancing group. A group of the latter type is present in poly (1-phosphonopropene) with units of the formula:

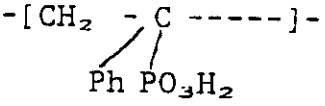
II 

A preferred phosphonic acid-containing AEA for use herein

is poly (beta styrene phosphonic acid) containing units of the formula:

III 

wherein Ph is phenyl, the phosphonic delivery-enhancing group and the phenyl retention-enhancing group being bonded on vicinal carbon atoms in the chain, or a copolymer of beta styrene phosphonic acid with vinyl phosphonyl chloride having the units of formula III alternating or in random association with units of formula I above, or poly (alpha styrene phosphonic acid) containing units of the formula:

IV 

in which the delivery - and retention - enhancing groups are geminally bonded to the chain.

These styrene phosphonic acid polymers and their copolymers with other inert ethylenically unsaturated monomers generally have molecular weights in the range of about 2,000 to about 30,000, preferably about 2,500 to about 10,000. Such "inert" monomers do not significantly interfere with the intended function of any copolymer employed as an AEA herein.

Other phosphonic-containing polymers include, for example, phosphonated ethylene having units of the formula.

V $-[(CH_2)_{14}CHPO_3H_2]_n-$

where n may for example be an integer or have a value giving

the polymer a molecular weight of about 3,000; and sodium poly (butene-4,4-diphosphonate) having units of the formula:

VI $-[CH_2 - CH----]-$
$CH_2 - CH < (PO_3Na_2)_2$ and

poly (allyl bis (phosphonoethyl amine) having units of the formula:

VII $-[CH_2 - CH---]-$
$CH_2 - N < (PO_3H_2)_2$

Other phosphonated polymers, for example poly (allyl phosphono acetate), phosphonated polymethacrylate, etc. and the geminal diphosphonate polymers disclosed in EP Publication 0321233 may be employed herein as AEA's, provided of course that they contain or are modified to contain the above-defined organic retention-enhancing groups.

As illustrative of AEA's containing phosphinic acid and/or sulfonic acid delivery enhancing groups, there may be mentioned polymers and copolymers containing units or moieties derived from the polymerization of vinyl or allyl phosphinic and/or sulfonic acids substituted as needed on the 1 or 2 (or 3) carbon atom by an organic retention-enhancing group, for example having the formula $-(X)_n-R$ defined above. Mixtures of these monomers may be employed, and copolymers thereof with one or more inert polymerizable ethylenically unsaturated monomers.

Illustrative of such monomers 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, and maleic acids and anhydrides. Other different olefinic monomer copolymerizable with such carboxylic monomers include vinylacetate, vinyl chloride, dimethyl maleate and the like. Copolymers contain sufficient salt groups for water-solubility.

As will be noted, in these and other polymeric AEA's operative herein, usually only one acidic delivery-enhancing group is bonded to any given carbon or other atom in the polymer backbone or branch thereon. Polysiloxanes containing or modified to contain pendant delivery-enhancing groups and retention enhancing groups may also be employed as AEA's herein. Also effective as AEA's herein are ionomers containing or modified to contain delivery-and retention-enhancing groups. Ionomers are described on pages 546-573 of the Kirk Othmer Encyclopedia of Chemical Technology, third edition, Supplement Volume, John Wiley & Sons, Inc. copyright 1984, which description is incorporated herein by reference. Also effective as AEA's herein, provided they contain or are modified to contain retention-enhancing groups, are polyesters, polyurethanes and synthetic and natural polyamides including proteins and proteinaceous materials such as collagen, poly (arginine) and other polymerized amino acids.

In the present invention a preferred oral composition is a dentifrice containing about 0.3% by weight of the antibacterial agent (e.g. triclosan) and about 1.5-2% by weight of the AEA.

Without being bound to a theory, it is believed that the AEA, especially polymeric AEA, is generally an anionic film forming material and is thought to attach to tooth surfaces and form a continuous film over the surfaces, thereby preventing bacterial attachment to tooth surfaces. It is possible that the noncationic antibacterial agent forms a complex or other form of association with the AEA, thus forming a film of a complex or the like over tooth surfaces. The film forming property of the AEA and the enhanced delivery and retention of the antibacterial agent on tooth surfaces due to the AEA appears to make tooth surfaces unfavourable for bacterial accumulation particularly since the direct bacteriostatic action of the antibacterial agent controls bacterial growth. Therefore, through the combination of three modes of actions: 1) enhanced delivery, 2) long retention time on tooth surfaces, and 3) prevention of bacterial attachment to tooth surfaces, the oral composition is made efficacious for reducing plaque. Similar antiplaque effectiveness is attained on soft oral tissue at or near the gum line.

In accordance with the present invention, the orally acceptable vehicle is effective to enable the substantially

water-insoluble noncationic antibacterial agent to dissolve in saliva in an effective antiplaque amount.

In the oral preparation, an orally acceptable vehicle includes a water-phase with humectant present. In a gel dentifrice, typically containing about 5-30% by weight of a siliceous polishing agent, water is typically present in amount of at least about 3% by weight, generally about 3-35%, and humectant, preferably glycerine and/or sorbitol typically total about 6.5-75% or 80% by weight of the oral gel dentifrice composition. Reference hereto to sorbitol refers to the material typically as available commerically in 70% aqueous solutions.

The gel dentifrices, when the amount of antibacterial agent is about 0.25-0.35% by weight, do not require a further ingredient in the oral vehicle to solubilize the antibacterial agent, although the presence of such solubilizing agent is optional. When the amount of antibacterial agent is below about 0.25% by weight, e.g. about 0.01 up to about 0.25% by weight, solubilizing agent therefore should be present in order to assure sufficient solubilization in saliva for antiplaque effectiveness. When the amount of antibacterial agent is above about 0.35% by weight, e.g. about 0.35 to about 0.5% or more, say 5%, solubilizing agent therefore should be present since otherwise a substantial part of the antibacterial agent would remain insoluble.

When the oral composition is a dentifrice containing about 30-75% by weight of a dentally acceptable polishing agent, the presence of such solubilizing agent is also optional.

when the oral composition is a mouthwash or liquid dentifrice, the oral vehicle includes at least one of a surface-active agent, a flavoring oil or a non-toxic alcohol each of which assists in dissolving the antibacterial agent and again the presence of such solubilizing agent is optional.

When solubilizing agent is present in oral compositions of the instant invention, it is typically in amount of about 0.5-20% by weight, with as little as about 0.5% by weight being sufficient when the amount of substantially water-insoluble non-cationic antibacterial agent is low, say up to about 0.3% by weight. When higher amounts such as least about 0.5% by weight of antibacterial agent are present and particularly when siliceous polishing agent is also present in amount of about 5-30% by weight, it is desirable that at least about 5% by weight, typically up to about 20% or more by weight, of the solubilizing agent be present. It is noted that there may be a tendency for the dentifrice to separate into liquid and solid portions when more than about 5% by weight of the solubilizing agent is present.

The agent which is or may be present to assist solubilization of the antibacterial agent in saliva may be incorporated in the water-humectant vehicle. Such solubilizing agents include humectant polyols such as propylene glycol, dipropylene glycol and hexylene glycol, cellosolves such as methyl cellosolve and ethyl cellosolve, vegetable oils and waxes containing at least about 12 carbons in a straight chain such as olive oil, castor oil and petrolatum and esters such as amyl acetate, ethyl acetate and benzyl benzoate. As used herein, "propylene glycol" includes 1,2-propylene glycol and 1,3-propylene glycol. Significant amounts of polyethylene glycol particularly of molecular weight of 600 or more should be avoided since polyethylene glycol effectively inhibits the antibacterial activity of the noncationic antibacterial agent. For instance, polyethylene glycol (PEG) 600 when present with triclosan in a weight ratio of 25 triclosan:1 PEG 600 reduces the antibacterial activity of triclosan by a factor of about 16 from that prevailing in the absence of the polyethylene glycol.

In accordance with aspects of this invention, oral compositions may be substantially gel in character, such as a gel dentifrice. Such gel oral preparations may contain siliceous dentally polishing material 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 or opacified 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 or alkali metal aluminosilicate complexes (that is, silica containing alumina combined in its matrix) are particularly useful, since they are consistant with gel-like texture and have refractive indices close to the refractive indices of gelling agent-liquid (including water and/or humectant) systems commonly used in dentifrices.

The polishing material is generally present in the oral composition dentifrices such as toothpaste or gel compositions in weight concentrations of about 5% to about 30%.

In the aspect of this invention wherein the oral preparation is a dentifrice, an orally acceptable vehicle including a water-phase with humectant which is preferably glycerine and/or sorbitol is present, wherein water is present typically in amount of about 15-35% or 40% by weight and glycerine and/or sorbitol typically total about 20-75% by weight of the oral preparation dentifrice, more typically about 25-60%. Reference hereto to sorbitol again refers to the material typically as available commercially in 70% aqueous solutions.

In this invention, the oral dentifrice composition may be substantially pasty in character, such as a toothpaste (dental cream), although when siliceous polishing agent is employed (which is not generally the case, since such material is typically not employed in amount above about 30% by weight) it can be gel in character. The vehicle of the oral composition dentifrice contains dentally acceptable polishing material, examples of which polishing materials are water-insoluble sodium metaphosphate, potassium mataphosphate, tricalcium phosphate, dihydrated dicalcium phosphate, anhydrous dicalcium phosphate, calcium carbonate, aluminum silicate, hydrated alumina, silica, bentonite, and mixtures thereof with each other or with hard polishing materials such as calcined alumina and zirconium silicate, material including the particulate thermosetting resins described in U.S. Pat. No. 3,070,510 issued Dec. 15, 1962, such as melamine- phenolic and urea-formaldehydes, and cross-linked polyepoxides and polyesters. Preferred polishing materials include insoluble sodium metaphosphates, dicalcium phosphate and hydrated alumina.

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 illustated 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 1% of the material is larger than 37 microns.

Hydrated alumina is an example of a polishing material which is essentially nonionic in nature. Typically, it is small in particle size, i.e., at least about 85% of the particules are smaller than 20 microns and is such as that classified as gibbsite (alpha alumina trihydrate) and normally represented chemically as $Al_2O_3.3H_2O$ or $Al(OH)_3$. The average particle size of gibbsite is generally about 6 to 9 microns. A typical grade has the following size distribution:

Micron	Percent
<30	94-99
<20	85-93
<10	56-67
< 5	28-40

The polishing material is generally present in the cream paste or gel compositions in weight contents of about 30% to about 75%.

Toothpastes or dental cream dentifrices as well as gel dentifrices 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%. A suitable thickener is 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 thickeners or gelling agents or thickeners include Irish moss, iota-carrageenan, gum tragacanth, starch, polyvinylpyrrolidone, hydroxyethpropyl-cellulose, hydroxybutyl methyl cellulose, hydroxypropyl methyl cellulose, hydroxyethyl cellulose (e.g. available as

Natrosol), sodium carboxymethyl cellulose, and particularly when siliceous polishing agent is present, colloidal silica such as those available as finely ground Syloid 244 or Sylodent 15.

In the aspect of the present invention wherein the oral composition is a mouthwash or liquid dentifrice, substantially liquid in character, the vehicle, particularly in a mouthwash, is typically a water-alcohol mixture. 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. The alcohol is a non-toxic alcohol such as ethanol or isopropanol. Humectant such as glycerine and sorbitol may be present in amount of about 10-30% by weight. Liquid dentifrices typically contain about 50-85% of water, may contain about 0.5-20% by weight of non-toxic alcohol and may also contain about 10-40% by weight of humectant such as glycerine and/or sorbitol. Reference here to sorbitol refers to the material typically as available commercially in 70% aqueous solutions. Ethanol is the preferred non-toxic alcohol. The alcohol is believed to assist in dissolving the water-insoluble non-cationic antibacterial agent as, it is believed also does flavoring oil.

As indicated, the noncationic antibacterial agent is substantially water-insoluble. However, in the present invention, with the AEA, such as polycarboxylate, present in the mouthwash or liquid dentifrice, organic surface-active agent, flavoring oil or non-toxic alcohol are believed to aid dissolving the antibacterial agent to assist it to reach soft oral tissue at or near the gums as well as tooth surfaces. Organic surface-active agents and/or flavoring oils may also assist dissolving the antibacterial agents as optional ingredients in oral dentifrice compositions.

Organic surface-active agents are also used in the compositions of the present invention to achieve increased prophylactic action, assist in achieving thorough and complete dispersion of the antiplaque antibacterial 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 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 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. Pluronic materials).

Surface active agent is typically present in amount of about 0.5-5% by weight, preferably about 1-2.5%.

When the oral composition is a liquid dentifrice the natural or synthetic thickener or gelling agent as described is typically present in proportions of about 0.1 to about 10%, preferably about 0.5 to about 5%.

Generally liquid dentifrices do not contain a polishing agent. However, as described in U.S. Patent 3,506,757 to Salzmann, about 0.3-2.0% by weight of a polysaccharide of high molecular weight in excess of 1,000,000 containing mannose, glucose, potassium glucuronate and acetyl moieties in the approximate ratio of 2:1:1:1, as suspending and thickening agent can be employed in a liquid dentifrice, which then may also contain about 10-20% of a polishing material such as hydrated alumina, dicalcium phosphate dihydrate, calcium pyrophosphate, insoluble sodium metaphosphate, anhydrous dicalcium phosphate, calcium carbonate, magnesium carbonate, magnesium oxide, silica, mixtures thereof, and the like.

Without being bound to a theory whereby the advantages of this invention are achieved, it is believed that an aqueous, humectant vehicle is normally solubilized in surfactant micelles in the mobile phase (that is, not including gelling agent and polishing agent, if present in a dentifrice formula). The mobile phase solution of dentifrice during use can become diluted with saliva which causes triclosan to precipitate. Thus, it is found that even in the absence of a special solubilizing material for

triclosan, when the amount of triclosan is about 0.25%-0.35% by weight and AEA such as the polycarboxylate is present, sufficient triclosan is present to exert an excellent antiplaque effect on the soft tissues at the gum line. Similar remarks apply to other water-insoluble noncationic antibacterial agents herein described.

The oral composition dentifrice may also contain a source of fluoride ions or fluorine-providing component, as anticaries agent in amount sufficient to supply about 25 ppm to 5000 ppm of fluoride ions. 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 substantial 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 flourosilicate, ammonium flourosilicate, sodium fluorozirconate, ammonium fluorozirconate, sodium monofluorophosphate, aluminum mono-and di-fluorophosphate and sodium calcium pyrophosphate. Alkali metal and tin fluorides, 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 prepartion, but it must be a non-toxic amount, generally about 0.0005 to about 3.0% in the preparation. In a dentifrice preparation, e.g. dental gel 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 sufficent compound to release about 300 to 2,000 ppm, more preferably 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 0.05% 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%.

It will be understood that, as is conventional, the oral preparations are to be sold or otherwise distributed in suitable labelled packages. Thus a dentifrice 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 dentifrice gel or the like.

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 incorporatd 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 are generally soluble and 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, euclyptus, majoram, cinnamon, lemon, and orange, and methyl salicylate. Suitable sweetening agents include sucrose, lactose, maltose, xylitol, sodium cyclamate, perillartine, AMP (aspartyl phenyl alanine, methyl ester), saccharine and the like. Suitably, flavor and sweetening agents may each or together comprise from about 0.1% to 5% or more of the preparation. Moreover, like the surface-active agent, flavoring oil is believed to aid the dissolving of the antibacterial agent, together with or even in the absence of surface-active agent.

In the preferred practice of this invention an oral composition of the present invention is preferably applied regularly to dental enamel and soft oral tissues, particularly at or near the gum line, such as every day or every second or third day or preferably from 1 to 3 times daily, at a pH of about 4.5 to about 9 or 10, generally about 5.5 to about 8, preferably about 6 to 8 and most preferably about 6.5 to about 7.5, for at least 2 weeks up to 8 weeks or more up to lifetime. Even at such pH below 5 enamel is not decalcified or otherwise damaged. 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.).

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 jelutong, 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, unless otherwise indicated.

EXAMPLE 1

The following dentifrice is prepared:

	Parts	
	A	B
Glycerine	10.00	-
Propylene Glycol	-	10.00
Sorbitol (70%)	25.00	25.50
Iota Carrageenan	0.60	0.60
AEA	2.00	2.00
Sodium Saccharin	0.40	0.40
Sodium Fluoride	0.243	0.243
Sodium Hydroxide (50%)	1.00	1.00
Titanium Oxide	0.50	0.50
Silica Polishing Agent (Zeodent 113)	20.00	20.00
Silica thickener (Sylox 15)	5.50	5.50
Sodium Lauryl Sulfate	2.00	2.00
Water	31.507	31.507
Triclosan	0.30	0.30
Flavor Oil	0.95	0.95

The AEA may be a polymer of alpha or beta-styrenephosphonic acid monomers or a copolymer of these monomers with each other or with other ethylenically unsaturated polymerizable monomers such as vinyl phosphonic acid.

The above dentifrice A delivers Triclosan to the teeth and soft gum tissue essentially as well as dentifrice B containing a special solubilizing agent for Triclosan. In other words, a special solubilizing agent is not required for the dentifrice of the present invention to be effective. Further, a corresponding dentifrice in which the AEA is absent is substantially poorer in delivering Triclosan.

In the foregoing example, improved results may also be obtained by replacing Triclosan with other antibacterial agents herein described such as phenol, thymol, eugenol and 2,2'-methylene bis (4-chloro-6-bromophenol).

EXAMPLE 2

The following liquid phase dentifrice solutions are tested for uptake and retention of triclosan on saliva coated HA disks following the test procedures described below with the indicated results:

Ingredients	PARTS			
	A	B	C	D
Sorbitol (70% solution)	30.0	30.0	30.0	30.0
Glycerol	9.5	9.5	9.5	9.5
Propylene Glycol	0.5	0.5	0.5	0.5
SLS	20.0	20.0	20.0	20.0
NaF	0.243	0.243	0.243	0.243
Flavor Oil	0.95	0.95	0.95	0.95
Triclosan	0.3	0.3	0.3	0.3
Water	56.507	54.507	54.507	54.507

Poly (beta-styrenephosphonic acid)		2.0		
Poly (alpha-styrenephosphonic acid)			2.0	
Polyvinyl Alcohol	———	———	———	2.0
Adjusted to pH 6.5 with NaOH				
Triclosan Uptake in Micrograms on Saliva Coated HA Disks	31.0	174.0	86.0	36.0
Retention of Triclosan on Saliva Coated HA Disks After:				
Initial		183.0		
30 minutes		136.0		
1 hour		105.0		
3 hours		83.0		

The above results show that solution (D) containing polyvinyl alcohol, not an AEA hereunder, produces a triclosan uptake of only 36.0, quite similar to the 31.0 uptake of the control solution (A) without additive. In contrast, solution (C) with poly (alpha-styrenephosphonic acid) produces an uptake of 86.0, more than double that of solutions (A) and (D), and solution (B) with poly (beta-styrenephosphonic acid) produces an uptake about 5 times that of solutions (A) and (D), tending to indicate further that vicinal substitution of the delivery-enhancing group yields superior results. The above results also show the surprisingly good retention of triclosan on the HA disks over time obtained with solution (B) containing poly (beta-styrenephosphonic acid (M.W's about 3,000 to 10,000).

The effect of AEA materials on the uptake, retention to and release from tooth surfaces of water-insoluble noncationic antibacterial agent is assessed in vitro on a saliva coated hydroxyapatite disk and on exfoliated buccal epithelial cells. The in vitro assessments are correlatable to in vivo delivery, and retention on oral surfaces.

For the test of delivery of antibacterial agent to a saliva coated hydroxyapatite disk, hydroxyapatite (HA) obtained from the Monsanto Co. is washed extensively with distilled water, collected by vacuum filtration, and permitted to dry overnight at 37°C. The dried HA is ground into a powder with a mortar and pestle. 150.00 mgs of HA are placed into the chamber of a KBr pellet die (Barnes Analytical, Stanford, CT.) and compressed for 6 minutes at 10,000 pound in a Carver Laboratory press. The resulting 13 mm disks are sintered for 4 hours at 800°C in a Thermolyne furnace. Parafilm stimulated whole saliva is collected into an ice-chilled glass beaker. The saliva is clarified by centrifugation at 15,000 Xg (times gravity) for 15 minutes at 4°C. Sterilization of the clarified-saliva is done at 4°C with stirring by irradiation of the sample with UV light for 1.0 hour.

Each sintered disk is hydrated with sterile water in a polyethylene test tube. The water is then removed and replaced with 2.00 ml of saliva. A salivary pellicle is formed by

incubating the disk overnight at 37°C with continuous shaking in a water bath. After this treatment, the saliva is removed and the disks are treated with 1.00 ml of a solution containing antibacterial agent (Triclosan) dentifrice liquid phase solution and incubated at 37°C with continuous shaking in the water bath. After 30 minutes, the disk is transferred into a new tube and 5.00 ml of water are added followed by shaking the disk gently with a Vortex. The disk is then transferred into a new tube and the washing procedure repeated twice. Finally, the disk is transferred carefully into a new tube to avoid co-transfer of any liquid along with the disk. Then 1.00 ml of methanol is added to the disk and shaken vigorously with a Vortex. The sample is left at room temperature for 30 minutes to extract adsorbed Triclosan into the methanol. The methanol is then aspirated and clarified by centrifugation in a Beckman Microfuge 11 at 10,000 rpm to 5 minutes. After this treatment, the methanol is transferred into HPLC (high performance liquid chromatography) vials for determination of antibacterial agent. Triplicate samples are used in all experiments.

For the test of retention of antibacterial agent to a saliva coated HA disk, a saliva coated HA disk is treated with dentifrice slurries as described above. After incubation or 30 minutes at 37°C, the HA disk is removed from the dentifrice slurry, washed twice with water, and then reincubated with parafilm stimulated human whole saliva which had been clarified by centrifugation. After incubation at 37°C with constant

shaking for various periods, the HA disk is removed from the saliva, and the amount of antibacterial agent (Triclosan) retained onto the disk and released into saliva is determined by analytical method using HPLC.

For the assay of delivery of antibacterial agent to buccal epithelial cells, the delivery is measured in order to determine the effect of PVM/MA on the delivery of antibacterial agent (Triclosan) to soft oral tissue from a dentifrice product. Buccal epithelial cells are collected with a wooden applicator stick by gently rubbing the oral mucosa. The cells are suspended in Resting Saliva Salts (Rss) Buffer (50 nM NaCl, 1.1 nM $CaCl_2$, and 0.6 nM KH_2PO_4 pH 7.0) to 5-6x10^5 cells/ml using a hemocytometer to enumerate the cells and kept in ice until use. 0.5 ml of cell suspension, preincubated to 37°C in a waterbath, is added with 0.5 ml of the test antibacterial agent solution and incubated at 37°C. The antibacterial agent solution in the incubation mixture is diluted at least 10 times in order to lower the surfactant concentration and prevent destruction of cell membranes by the surfactant. After 30 minutes of incubation, the cells are harvested by centrifugation in Beckman Microfuge 11 at 5,000 rpm for 5 minutes. The cells, collected as the pellet, are washed 3 times with RSS buffer and treated with 1.5 ml of methanol. The sample is mixed vigorously and is analyzed for antibacterial agent by the HPLC method.

EXAMPLE 3

The following dentifrices of the invention are prepared:

	Parts	
	A	B
Glycerine	-	20.00
Propylene Glycol	10.00	0.50
Sorbitol (70%)	25.00	19.50
Sodium Carboxymethyl Cellulose	-	1.10
Iota Carrageenan	0.600	-
Sodium Saccharin	0.40	0.30
Sodium Fluoride	0.243	0.243
Silica Polishing Agent (Zeodent 113)	20.00	20.00
Silica thickener (Sylox 15)	5.50	3.00
Water	28.757	15.307
AEA	2.00	2.00
Triclosan	0.50	0.30
Titanium Dioxide	0.50	0.50
Sodium Lauryl Sulfate	2.50	2.00
Flavor	1.10	0.95
Ethanol	1.00	-
Sodium Hydroxide (50%)	2.00	1.60

The AEA may be a polymer of monomeric alpha- or beta-styrene phosphonic acid or a copolymer of these styrene phosphonic acid monomers with each other or with other ethylenically unsaturated polymerizable monomers such as vinyl phosphonic acid.

In the foregoing examples, improved results may also be obtained by replacing Triclosan with other antibacterial agents herein described such as phenol, thymol, eugenol and 2,2'methylene bis (4-chloro-6-bromophenol).

EXAMPLE 4

The following antiplaque dentifrice is prepared:

	Parts
Glycerine	15.00
Propylene Glycol	2.00
Sodium Carboxymethyl cellulose	1.50
Water	24.93
AEA	4.76
Sodium Monofluorophosphate	0.76
Sodium Saccharin	0.30
Insoluble Sodium Metaphosphate	47.00
Titanium Dioxide	0.50
Sodium Lauryl Sulfate	2.00
Triclosan	0.30
Flavor	0.95

The AEA may be a styrene phosphonic acid polymer having molecular weight within the range of about 3,000 to 10,000 such as poly (beta-styrenephosphonic acid), a copolymer of vinyl phosphonic acid with beta-styrenephosphonic acid, or poly (alpha-styrenephosphonic acid), or a sulfoacrylic oligomer.

In the foregoing examples improved results are also achievable when Triclosan is replaced with each of phenol, 2,2'-methylene bis (4-chloro-6-Bromophenol), eugenol and thymol.

EXAMPLE 5

The following liquid dentifrices are also effective in reducing plaque by increasing the uptake and retention of Triclosan on oral surfaces:

	A Parts	B Parts	C Parts
Glycerine	20.0	20.0	-
AEA	0.3	0.3	0.3
Polysaccharide of high molecular weight, the molecule containing mannose, glucose, potassium glucuronate and acetyl moieties in the approximate molar ratio of 2:1:1:1	0.8	-	1.0
Sodium benzoate	0.5	0.5	0.5
Saccharine sodium	0.5	0.5	0.5
Water	61.3	73.1	71.6
Sodium lauryl sulfate	3.0	3.0	3.0
Insoluble sodium metaphosphate	10.0	-	10.0
Anhydrous dicalcium phosphate	1.0	-	2.5
Flavoring Oil	2.5	2.5	2.5
Ethyl alcohol	-	-	10.0
Triclosan	0.1	0.1	0.1

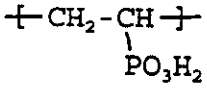
In the forgoing Examples, improved results are also achievable when Triclosan is replaced with each of phenol, 2,2'-methylene bis (4-chloro-6-Bromophenol), eugenol and thymol. The AEA may be a styrene phosphonic acid polymer having molecular weights within the range of about 3,000 to 10,000 such as poly (beta-styrenephosphonic acid), a copolymer of vinyl phosphonic acid with beta-styrenephosphonic acid, or poly (alpha-styrenephosphonic acid), or a sulfoacrylic oligomer.

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.

Attention is directed to our copending GB Application No. 8928878.1, Serial No. 2227660, which claims an oral composition comprising an effective antiplaque amount of a substantially water insoluble noncationic antibacterial agent, 0.005-4% by weight of antibacterial enhancing agent which enhances delivery of said antibacterial agent to, and retention on, oral surfaces and an orally acceptable vehicle effective to enable the said antibacterial agent to dissolve in saliva in effective antiplaque amount, the said oral composition being free of polyphosphate anticalculus agent.

Attention is also directed to our copending GB Application No. 9225278.2, Serial No. 2259886, which is divided from GB 8928878.1 and which claims an oral composition comprising an effective antiplaque amount of a substantially water insoluble non-cationic antibacterial agent, 0.005 to 4% by weight of an antibacterial-enhancing agent which enhances the delivery of the said antibacterial agent to oral surfaces, and an orally acceptable vehicle effective to enable the said antibacterial agent to dissolve in saliva in an effective antiplaque amount, the said oral composition being free of polyphosphate anticalculus agent, the antibacterial enhancing agent being a poly(vinyl phosphonic acid) containing units of the formula



the composition having a pH in the range 4.5-10.

CLAIMS

1. An oral composition comprising an orally acceptable vehicle, an effective antiplaque amount of a substantially water-insoluble non-cationic antibacterial agent and an antibacterial-enhancing agent which has an average molecular weight of 1,000 to 1,000,000, and contains at least one delivery enhancing functional group and at least one organic retention enhancing group, the said agent containing the said groups being free from or substantially free from water soluble alkali metal or ammonium synthetic anionic linear polymer polycarboxylate salt having a molecular weight of 1,000 to 1,000,000, the said oral composition being free of polyphosphate anticalculus agent.

2. An oral composition as claimed in Claim 1 in which the said antibacterial agent is present in amount of from 0.25% to less than 0.5% by weight.

3. An oral composition as claimed in Claim 1 in which the said antibacterial agent is present in amount of from 0.25% to 0.35% by weight.

4. An oral composition as claimed in Claim 1, 2 or 3 in which the said oral composition contains a siliceous polishing agent.

5. An oral composition as claimed in any one of Claims 1 to 4 comprising 0.005-4% by weight of antibacterial enhancing agent which enhances delivery of said antibacterial agent to, and retention on, oral surfaces.

6. An oral composition as claimed in any one of Claims 1 to 5 in which the said oral composition is a dentifrice comprising 5-30% by weight of a siliceous polishing agent and the said antibacterial agent is present in amount of 0.25-0.35% by weight and there is present at least one of a surface-active agent and a flavouring oil.

7. An oral composition as claimed in any one of Claims 1 to 5 in which the said oral composition is a dentifrice comprising 5-30% by weight of a siliceous polishing agent, the said antibacterial agent is present in amount of 0.01-5% by weight and the said oral composition comprises a solubilizing material in amount sufficient to dissolve the said antibacterial agent in saliva.

8. An oral composition as claimed in any one of Claims 1 to 7 in which the said oral composition is a dentifrice comprising 30-75% by weight of a dentally acceptable water-insoluble polishing agent.

9. An oral composition as claimed in any one of Claims 1 to 3 in which the said oral composition is a mouthwash or liquid dentifrice and the said orally acceptable vehicle is an aqueous vehicle wherein there is present at least one of a surface-active agent, a flavouring oil or a non-toxic alcohol.

10. An oral composition as claimed in any one of the preceding claims in which there is present surface-active agent in amount of 0.5-5% by weight.

11. An oral composition as claimed in any one of the preceding claims in which there is present flavouring oil in amount of 0.1-5% by weight.

12. An oral composition as claimed in Claim 9 in which the said composition is a mouthwash and the said aqueous vehicle contains ethanol and the weight ratio of water to ethanol is from 1:1 to 20:1.

13. An oral composition as claimed in Claim 9 or Claim 12 in which the said oral composition is a liquid dentifrice containing 0.3-2.0% by weight of a polysaccharide of high molecular weight in excess of 1,000,000 containing mannose, glucose, potassium glucuronate and acetyl moieties in the approximate ratio of 2:1:1:1, as suspending and thickening agent and 10-20% by weight of a polishing material.

14. An oral composition as claimed in any of Claims 1 to 13 in which the said antibacterial agent is selected from the group consisting of halogenated diphenyl ethers, halogenated salicylanilides, benzoic esters, halogenated carbanilides and phenolic compounds.

15. An oral composition as claimed in Claim 14 in which the said antibacterial agent is a halogenated diphenyl ether.

16. An oral composition as claimed in Claim 15 in which the said halogenated diphenyl ether is 2,4,4'-trichloro-2'-hydroxyphenyl ether.

17. An oral composition as claimed in any one of Claims 1 to 16 in which a solubilizing agent is present

in amount of 0.5 to 20% by weight and is selected from the group consisting of propylene glycol, dipropylene glycol, hexylene glycol, methyl cellosolve, ethyl cellosolve, vegetable oil and wax containing at least 12 carbon atoms, amyl acetate, ethyl acetate, glyceryl tristearate and benzyl benzoate.

18. An oral composition dentifrice as claimed in Claim 17 in which the solubilizing agent is propylene glycol and is present in amount of about 0.5% by weight.

19. An oral composition in the form of a dentifrice as claimed in any one of Claims 1 to 18 wherein a polishing agent is present which is selected from the group consisting of sodium metaphosphate, tricalcium phosphate, dihydrated dicalcium phosphate, anhydrous dicalcium phosphate, calcium pyrophosphate, magnesium orthophosphate, trimagnesium phosphate, calcium carbonate, aluminum silicate, hydrated alumina, silica, bentonite and mixtures thereof.

20. An oral composition dentifrice as claimed in Claim 19 wherein said polishing agent is dicalcium phosphate dihydrate or hydrated alumina.

21. An oral composition as claimed in any one of Claims 1 to 20 in which the said delivery-enhancing group is acidic.

22. An oral composition as claimed in Claim 21 in which the said delivery-enhancing group is selected from the group consisting of carboxylic, phosphonic, phosphinic, and sulfonic acids, and their salts, and mixtures thereof.

23. An oral composition as claimed in any one of Claims 1 to 22 in which the said organic retention-enhancing group comprises the formula $(X)_n$-R wherein X represents O, N, S, SO, SO_2, P, PO or Si, R represents a hydrophobic alkyl, alkylene, acyl, aryl, alkaryl, aralkyl, or heterocyclic group, or their inert-substituted derivatives, and n is 1 or zero.

24. An oral composition as claimed in any one of Claims 1 to 23 wherein the said antibacterial-enhancing agent is an anionic polymer containing a plurality of the said delivery-enhancing and retention-enhancing groups.

25. An oral composition as claimed in Claim 24 in which the said anionic polymer comprises a chain containing repeating units each containing at least one carbon atom.

26. An oral composition as claimed in Claim 25 in which each unit contains at least one delivery-enhancing group bonded to the same, vicinal, or other atoms in the chain.

27. An oral composition as claimed in any one of Claims 22 to 26 in which the delivery-enhancing group is a carboxylic group of salt thereof.

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Title ANTIPLAQUE ANTIBACTERIAL ORAL COMPOSITION

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