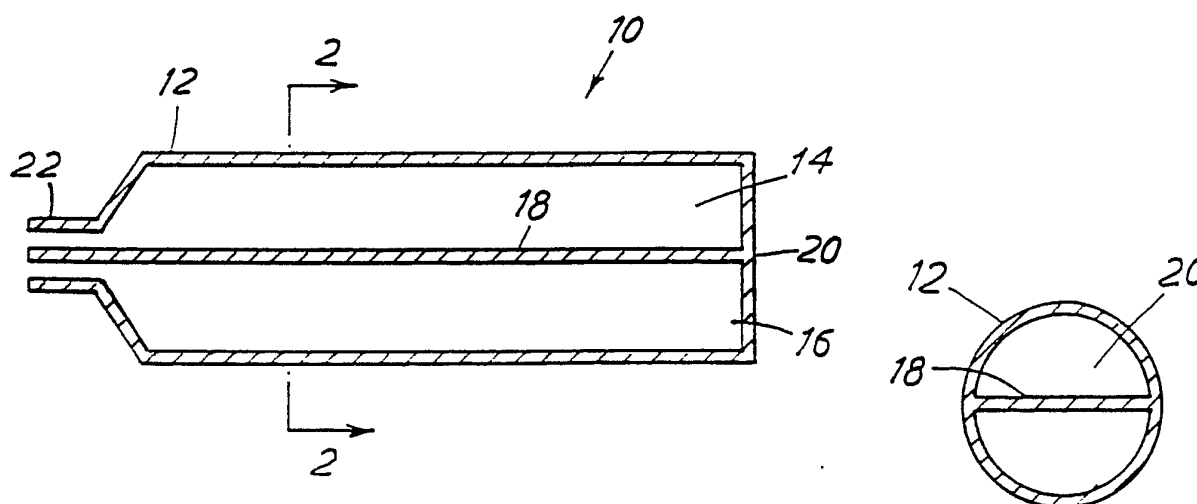


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(54) Title: DESENSITIZING DENTAL COMPOSITION



(57) Abstract

Compositions are provided for relieving tooth hypersensitivity in which one or more specifically formulated compositions are applied to the tooth surface. The compositions contain ionic species which result in the formation of precipitates within the enamel tubules with the formation of precipitated salts or other compounds having a particularly low solubility either on in situ mixing of cations and anions, or on reaction with oral liquids. Formation of low-solubility compounds leads to increased deposition of these compounds on tooth surfaces and in dentinal tubules which can lead to dentinal desensitisation.

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DESENSITIZING DENTAL COMPOSITION

This invention relates to a desensitizing dental composition.

Hypersensitivity is a common phenomenon among dental patients that often causes the patient to reject dental treatment.

The sensitivity may be local or general and very often complicates treatment of a variety of dental problems. Treatment of hypersensitivity has resulted in varying degrees of success. The treatment often has relied upon the astringent or coagulating effects of various agents, occluding properties or the ability to render calcium less soluble. Examples of these agents include formaldehyde, silver nitrate, zinc oxide and strontium chloride.

It has been considered hitherto that the ability of strontium ions to exert an anti-hypertensive effect would be negated if the strontium ions were converted to a relatively insoluble form. Thus, according to my International patent Application No W087/02890, a system was provided for applying separate sources of soluble strontium ions and fluoride ions to the surface of teeth in which the separate sources were admixed on or immediately prior to application to the tooth surface in order to prevent or delay the formation of relatively insoluble species which would make both the strontium and fluoride ions unavailable for interaction with the tooth surface.

It has now been determined that tooth hypersensitivity can be countered by applying one or more specifically formulated compositions to the tooth surface, which compositions contain ionic species which result in the formation of precipitates within the enamel tubules with the formation of precipitated salts or other compounds having a particularly low solubility. Thus according to the invention, in situ mixing of cations and anions, or reaction with oral liquids, leads to the formation of low-solubility compounds leading to increased deposition of these compounds on tooth surfaces and in dentinal tubules which can lead to dentinal desensitisation.

More specifically, the present invention provides a system allowing the accelerated deposition of calcium and/or strontium salts in or near the dentinal tubules of the tooth in order to alleviate the pain of dental sensitivity.

This accelerated deposition may be achieved by in situ formation of low solubility compounds in two ways:

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(1) The mixing immediately prior to or at the time of administration to the oral cavity of two solutions containing respectively either calcium and/or strontium and an appropriate anion.

(2) The administration to the oral cavity of a solution containing calcium and/or strontium and a suitable anionic component, which upon interaction with oral liquids such as saliva, can decompose to form an anionic species which can lower the solubility of the strontium and/or calcium. As an example is cited the decomposition of sodium monofluorophosphate (NaMFP) to fluoride and phosphate under the influence of salivary components. This fluoride and/or phosphate will react with Ca^{2+} and/or Sr^{2+} and lower the solubility of these cations leading to accelerated deposition in or around the dentinal tubules.

Thus in accordance with a first aspect of this invention (Variant 1), there is provided a system for preparing a desensitizing composition, said system comprising a source of a first cationic species and a source of a second anionic species, both sources being in physiologically acceptable form and said sources being segregated from each other, said first ionic species being selected from calcium and/or strontium ions and said second ionic species being selected from anions which combine with the first ionic species to form a salt whose solubility is less than 10 mg in 100 ml of cold water. There is also provided a dispensing means arranged to dispense said sources of ions so that a mixture thereof may be formed on, or immediately prior to application (of the composition) to, the teeth.

In accordance with a second aspect of the invention (Variant 2) a desensitising composition is provided comprising a physiologically acceptable source of strontium and/or calcium ions and a physiologically acceptable source of a suitable anion, the anions being bound in a form such that the sources are unreactive with each other at ambient conditions (e.g. during storage) but upon reaction with oral liquids such as saliva a precipitate of a salt or other compound of the anion and cation is formed.

In this embodiment it is preferred, but not essential, for the precipitate to have a solubility of less than 10 mg in 100 ml of cold water.

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It will be understood that with this modified form of the invention, the sources of cation and anion do not have to be kept apart from each other prior to use.

More specifically in accordance with the first aspect of the invention there is provided a package which houses a dental desensitising composition which includes a physiologically acceptable source of strontium and/or calcium ions and a physiologically acceptable source of anion as described above, wherein these two sources are maintained separate from each other and are not admixed until application to the teeth is desired. Thus for example, when the sources are mixed in situ on the tooth surface, a precipitate may be formed whose action is desensitizing.

The package may include compartments, one for housing the calcium and/or strontium ions in the absence of said specified anion, and the other for housing the specified anion, preferably in the absence of calcium and/or strontium ions. The said sources of ions can then be dispensed simultaneously on the teeth surfaces.

In the past, dentinal desensitizing compositions have been formulated using alkaline earth metals, but always in the form of soluble salts. It was felt that insoluble salts would act only as abrasives and could not provide the cation species necessary for deposition in, or in the proximity of, the dentinal tubule. It has now been found in accordance with this invention however, that in situ formation of low solubility salts in the process of dental desensitization can be effective. It is postulated that in the present invention the desensitizing action occurs due to the formation of particles, e.g. crystals, of insoluble precipitate inside the dentinal tubules, thereby blocking them. Thus, advantageously, the calcium or strontium ion and the anion, respectively, are provided in their respective sources in concentrations such that upon mixing small particles can be formed in the tubules in a suitably short time, i.e. before the reagent diffuses out.

Physiologically safe reagents should be used as the sources of the ions to form the precipitates.

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Examples of acceptable anions that may be employed to obtain with calcium and/or strontium, precipitates of the required low solubility include fluoride, orthophosphate, pyrophosphate, metaphosphate, carbonate and oxalate; it being understood that not all these anions are suitable with both cations; for example the solubility of strontium fluoride is above 11 mg per 100 ml in cold water. The approximate solubilities of some of the preferred salts in 100 ml of cold water are given below:

Calcium Fluoride	1.6 mg
Calcium Orthophosphate	2-3 mg
Calcium Metaphosphate	Insoluble
Calcium Pyrophosphate	Insoluble
Calcium Oxalate	0.67 mg
Strontium Carbonate	1.1 mg
Strontium Oxalate	5.1 mg
Strontium Orthophosphate	Highly insoluble

Strontium fluoride (which may be formed as a precipitate on admixing separate compositions containing strontium ions as the sole cationic species and fluoride ions as the sole anionic species, e.g. as described in my previous International Patent Application No WO87/2890) has a solubility of around 11 mg/100ml. Accordingly compositions which on use result in the formation of strontium fluoride as the sole low-solubility salt do not form part of Variant (1) the present invention. The formation of strontium fluoride is however encompassed by Variant (2).

The invention further provides a kit for desensitizing the dental area of a patient having hypersensitive teeth which comprises supplies of two separate dentifrice or mouthwash compositions, one of said compositions containing a source of a physiologically acceptable free calcium and/or strontium ion and the other of said compositions containing a physiologically acceptable source of free anion, and optionally instructions for admixing said compositions on or immediately prior to application to the teeth of the patient in order to achieve desensitization.

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The invention also provides the use of a physiologically acceptable source of strontium and/or calcium cations to produce industrially a kit or system for the treatment of teeth in a combination therapy involving the application of said cations and anions which will combine with the chosen cations to produce a precipitate having a solubility of less than 10 mg in 100 ml of cold water, using separate compositions containing respectively said cations and said anions.

The invention further provides the use of a physiologically acceptable source of anions to produce industrially a kit or system for the treatment of teeth in a combination therapy involving the application of said anion and cations selected from calcium and/or strontium ions which will combine with the chosen anion to produce a precipitate having a solubility of less than 10 mg per 100 ml of cold water using separate compositions containing respectively said anions and said cations.

Any convenient means for effecting separation of the source of calcium and/or strontium ions and the source of the prescribed anion according to the first aspect of the invention can be utilized. For example, a single container may be compartmentalized so that the calcium and/or strontium containing source and the anion containing source are housed in separate compartments and are not admixed until applied to the teeth or immediately before such application. Alternatively, the segregating means may comprise a physiologically acceptable composition located between and separating the two sources in a single compartment and adapted to be dispensed with said segregated ion-containing phases.

The calcium and/or strontium containing source is preferably maintained at a pH of between about 3 and about 7 more preferably between about 5 and 7 so that the calcium and/or strontium ions are solubilized within the source at the desired concentration. The preferred sources of strontium and calcium are strontium and calcium chlorides since they are readily dissolved in an aqueous medium. The sources of the strontium and/or calcium ions and the anion are most conveniently each maintained in a viscous aqueous medium such as in the form of a gel or a paste.

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I. PROPOSED FORMULATIONS

The preferred concentration ranges for the active ingredients are as follows (most preferred concentrations in brackets).

1. Biphasic formulationsCationic phase:

SrCl ₂ .6H ₂ O	0.01 % - 20 %	(1 % - 10 %)
CaCl ₂ .2H ₂ O	0.01 % - 20 %	(1 % - 10 %)

Anionic phase:

NaF	0.01 % - 2 %	(0.1 % - 1 %)
NaMFP	0.05 % - 5 %	(0.1 % - 1 %)
K ₂ HPO ₄	0.01 % - 5 %	(1 % - 3 %)
K ₂ CO ₃	0.01 % - 5 %	(1 % - 3 %)
Na ₂ SO ₄	0.01 % - 5 %	(1 % - 3 %)

2. Single-phase formulation

SrCl ₂ .6H ₂ O	0.01%-10% (1%-5%)	+NaMFP 0.05%-5% (0.05%-0.5%)
CaCl ₂ .2H ₂ O	0.01%-10% (1%-5%)	+NaMFP 0.05%-5% (0.05%-0.5%)

It is understood that soluble salts of strontium, calcium, fluoride, fluorophosphate, phosphate, carbonate or sulfate other than the ones given as examples can be used in the formulations.

It is most preferred that the strontium and/or calcium and the chosen anion be present in either a toothpaste composition suitable for cleaning teeth, in a mouthwash with desensitizing properties, or in a gel composition of the type commonly used by dentists in order to apply treatment compositions to the teeth or gum surface.

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Thus for example, in addition to the active ingredients the compositions of this invention may also contain other excipients. These are chosen such that they interfere minimally with the active ingredients. For example, anionic binding agents are preferably avoided

The toothpaste formulations may contain abrasive, binding agents, humectants, thickening agents, surfactants, preservative, flavouring agents, sweetening agents, anti-bacterial agents, colouring agents, anti-corrosive agents, pH-adjusters and anti-plaque additives.

Mouthwash formulations may contain humectants, alcohol, flavouring agents, sweetening agents, preservatives, antibacterial agents, colouring agents, pH-adjusters, anti-plaque additives and surfactants.

Where the compositions used in accordance with the invention contain abrasives, the abrasive may be synthetic silicas or derivatives thereof, e.g. a precipitated silica, or an alkaline earth metal carbonate. The abrasive is generally present in an amount of 10 to 60% by weight of the composition.

The composition of the invention may include one or more non-ionic binding agents, such as hydroxy ethylcellulose, or xanthan gums. These binding agents may be present in an amount, for example of 0.1% to 5% by weight of the composition.

The compositions may also include one or more humectants in a total amount, for example of up to 90% by weight of the composition. Examples of such humectants include glycerin, sorbitol syrup, polyethylene glycols and propylene glycol.

The composition may include thickening agents in an amount for example of up to 20%, preferably 0.5% to 10% by weight of the composition. Examples of thickening agents include pyrogenic silica and natural and synthetic clays, such as hydrated sodium magnesium lithium silicates.

It is usually desirable to include a a ionic organic surfactant in the composition. These surfactants are usually present in an amount of, for example 0.5% to 10%, preferably 1% to 5%, by weight of the composition.

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The compositions may also include one or more preservatives for example benzoic acid, methyl *p*-hydroxybenzoate or sodium benzoate. The preservatives may be present in an amount, for example up to 5%, preferably 0.05% to 1%, by weight of the composition. Chloroform may alternatively or additionally be included as a preservative in an amount, for example, of up to 5%, preferably 0.1% to 2%, by weight of the composition. Chloroform also acts as a flavouring agent.

Other flavouring agents may be included in an amount, for example of up to 5%, preferably 0.5% to 2%, by weight of the composition. Examples of flavouring agents include conventional flavouring oils, such as oils of spearmint, peppermint, wintergreen and cloves. Sweetening agents, especially saccharin, may additionally or alternatively be included in an amount, for example of up to 5%, preferably 0.1% to 1% by weight of the composition.

The compositions may also include anti-bacterial agents in an amount of, for example up to 5%, preferably 0.1% to 1%, by weight of the composition. A particularly suitable anti-bacterial agent is chlorhexidine (1,1'-hexamethylene-bis-[5-(4-chlorophenyl)biguanide]).

The compositions may also include anti-plaque additives, e.g. sparingly water-soluble zinc salts, especially zinc citrate, in an amount for example of from 0.25% to 10% by weight of the composition. Other anti-plaque additives that may be used include xylitol and 8-hydroxyquinoline and derivatives thereof, e.g. 4,5-dimethyl and 5-methoxy-4-methyl-8-hydroxyquinoline.

Other additives may include one or more of colouring agents; anti-corrosive agents, e.g. sodium silicate; pH adjusters, e.g. citric acid. Each of these agents may be present in amounts, for example of up to 2%, preferably 0.1% to 1%, by weight of the composition.

The compositions are usually aqueous compositions and include water in an amount of up to, for example 50%, preferably 10% to 30%, by weight of the composition.

When it is desirable to form the ion containing sources of the invention as gels, an aqueous solution of the ion may be admixed with a pharmaceutically acceptable gelling agent such as sodium carboxymethyl cellulose, hydroxyethyl cellulose, hydroxypropyl cellulose, magnesium aluminium silicate, silica gel or the like. The

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thixotropic properties of the resultant gel can be varied by varying the concentration of the gelling agent, with increased concentrations providing increased thixotropic properties as is well known in the art.

When it is desired to form the calcium and/or strontium containing source and the anion containing source as aqueous solutions, such as could be used as a mouthwash, separate aqueous solutions of calcium and/or strontium and of the anion may, for example, be enclosed in a two-compartment bottle in accordance with the first aspect of the invention from which both solutions can be dispensed simultaneously immediately prior to use as a mouthwash.

The compositions utilized in the present invention are conveniently formed by first preparing an aqueous solution of either the calcium and/or strontium compound or the prescribed anion compound, preferably in deionized water. The concentration of the calcium and/or strontium compound may be such that in the final composition it comprises between 0.01 and 20 weight per cent of the final composition (exclusive of the prescribed anion-containing composition), preferably between 1 and 10 weight percent. Similarly the prescribed anion-containing composition in the aqueous solution may be such that concentration in the final composition is between 0.01 and 5 weight percent (exclusive of the calcium and/or strontium containing phase), more preferably between 0.1 and 3 weight percent. After the aqueous solution has been formed, the conventional agents utilized to form a paste or a gel or the like may then be admixed with the aqueous solution to form the final composition.

Referring to Figures 1 and 2, a suitable container (10) useful for housing said first and second sources in accordance with the first aspect of the present invention comprises an outer wall formed of a flexible material such as a polymer which can contain a sheet of flexible metal such as aluminium (12). The container (10) is segmented into two compartments (14) and (16) by means of a wall (18) which is sealed to the interior surface of the outer wall (12). One end (20) of the container is sealed while the opposing end (22) is open so that it can be conveniently opened or closed in a conventional manner such as with a screw cap (not shown). Compartment (14) can

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house either the cation-containing source or the anion-containing source while the other compartment (16) can house the source not housed within compartment (14).

It is to be understood that in accordance with the first aspect of the invention, alternatively the calcium and/or strontium containing source and the anion-containing source can be housed in separate containers from which they can be conveniently dispensed just prior to being topically applied to the dental area of the user. In yet another alternative, an intermediate layer of toothpaste, gel or the like containing neither cation nor anion can be interposed between the layer of calcium and/or strontium source and the layer of anion source within the same container so that mixture of the ion containing layers does not occur until use.

It will also be understood that, in accordance with the second aspect of the invention, the cation and anion containing sources can be housed together in a container with a single compartment as is used commonly for mouthwashes, gels and toothpaste, because precipitate formation does not occur until the anion is released from its chemically bound form by contact with oral liquids.

The following experimental results demonstrate the effect of selecting different pairs of anions and cations on the nature and rate of formation of insoluble salts in accordance with the invention.

II. EXPERIMENTAL

1. Different bi-phasic formulations

Aqueous solutions were made of 10% $\text{SrCl}_2 \cdot 6\text{H}_2\text{O}$, 10% $\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$, 1% NaF , 1% NaFPO_3 , 3% K_2HPO_4 , 3% K_2CO_3 and 3% Na_2SO_4 .

5ml of either the $\text{SrCl}_2 \cdot 6\text{H}_2\text{O}$ solution or the $\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$ solution was mixed with 5ml of the solutions of either the NaF , NaFPO_3 , K_2HPO_4 , K_2CO_3 or Na_2SO_4 solutions. The rate of precipitation was observed and the following conclusions were drawn:

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<u>Mixture</u>	<u>Result</u>
$\text{Sr}^{2+} + \text{F}^{-}$	Dense, well formed precipitate
$\text{Ca}^{2+} + \text{F}^{-}$	faintly turbid suspension, deepening quickly
$\text{Sr}^{2+} + \text{FPO}_3^{-}$	very little precipitate, caused by free fluoride and phosphate
$\text{Ca}^{2+} + \text{FPO}_3^{-}$	very faint turbidity, caused by free fluoride and phosphate
$\text{Sr}^{2+} + \text{HPO}_4^{2-}$	paint-like precipitate
$\text{Ca}^{2+} + \text{HPO}_4^{2-}$	paint-like precipitate
$\text{Sr}^{2+} + \text{CO}_3^{2-}$	paint-like precipitate
$\text{Ca}^{2+} + \text{CO}_3^{2-}$	dense, well formed precipitate
$\text{Sr}^{2+} + \text{SO}_4^{2-}$	thick precipitate
$\text{Ca}^{2+} + \text{SO}_4^{2-}$	slowly setting, crystalline deposit

2. Single-phase preparation

An aqueous solution of 10% $\text{SrCl}_2 \cdot 6\text{H}_2\text{O}$ was mixed with an equal volume of an aqueous solution of 1% NaMFP (NaFPO_3).

The resulting fine precipitate was allowed to settle overnight and filtered off.

The supernatant remains stable for weeks. 10ml samples are then mixed with 0.5ml of saliva.

A precipitate forms rapidly and is heavy within five minutes. Even in a four-fold diluted solution, the saliva causes a precipitate to form.

As a blank, individual solutions of 5% $\text{SrCl}_2 \cdot 6\text{H}_2\text{O}$ and 0.5% NaMFP were mixed with a 0.5ml of saliva. No precipitation occurred. This indicates that in the mixtures of $\text{SrCl}_2 \cdot 6\text{H}_2\text{O}$ and NaMFP the precipitate occurs through the interaction of Sr(II) and phosphate or fluoride, which had been liberated by the action of salivary components on NaMFP.

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The following oral desensitizing compositions, which are embodiments of this invention, are set forth in the following examples which are given to illustrate the present invention:

Biphatic toothpaste

1. Cationic phase (containing $\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$)

<u>Ingredient</u>	<u>% by weight</u>
$\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$	10.000
Abrasive (precipitated silica gel)	20.000
Sorbitol (30% in H_2O)	20.000
Glycerin	10.000
Hydroxyethylcellulose	1.000
Sodium alkyl sulfate (28% in H_2O)	4.000
Saccharin	0.300
Titanium dioxide	0.500
Flavour	1.000
Colour	0.700
Chlorohexidine	0.500
Methylparaben	0.060
Propylparaben	0.020
Water	Balance

2. Anionic phase

<u>Ingredient</u>	<u>% by weight</u>
NaF	0.200
Abrasive (precipitated silica gel)	20.000
Sorbitol (30% in H_2O)	20.000
Glycerin	10.000
Hydroxyethylcellulose	1.000
Sodium alkyl sulfate (28% in H_2O)	4.000
Saccharin	0.300
Titanium dioxide	0.500
Chlorhexidine	0.500
Methylparaben	0.060
Propylparaben	0.020
Flavour	1.000
Colour	0.700
Water	Balance

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2. Cationic phase (containing $\text{SrCl}_2 \cdot 6\text{H}_2\text{O}$)

<u>Ingredient</u>	<u>% by weight</u>
$\text{SrCl}_2 \cdot 6\text{H}_2\text{O}$	10.000
Abrasive (precipitated silica gel)	20.000
Sorbitol (30% in H_2O)	20.000
Glycerin	10.000
Hydroxyethylcellulose	1.000
Sodium alkyl sulfate (28% in H_2O)	4.000
Saccharin	0.300
Titanium dioxide	0.500
Flavour	1.000
Colour	0.700
Chlorohexidine	0.500
Methylparaben	0.060
Propylparaben	0.020
Water	Balance

2. Anionic phase

<u>Ingredient</u>	<u>% by weight</u>
Na_2HPO_4	0.200
Abrasive (precipitated silica gel)	20.000
Sorbitol (30% in H_2O)	20.000
Glycerin	10.000
Hydroxyethylcellulose	1.000
Sodium alkyl sulfate (28% in H_2O)	4.000
Saccharin	0.300
Titanium dioxide	0.500
Chlorhexidine	0.500
Methylparaben	0.060
Propylparaben	0.020
Flavour	1.000
Colour	0.700
Water	Balance

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Biphasic mouthwash1. Cationic phase (CaCl₂.2H₂O)

<u>Ingredient</u>	<u>% by weight</u>
CaCl ₂ .2H ₂ O	10.000
Glycerin	10.000
Ethanol (190 proof, USP)	7.500
Flavour	0.500
Sodium saccharin	0.100
Chlorhexidine	0.500
Methylparaben	0.060
Propylparaben	0.020
Colouring agent	0.300
Water	Balance

2. Anionic phase

NaF	0.200
Glycerin	10.000
Ethanol (190 proof, USP)	7.500
Flavour	0.500
Sodium saccharin	0.100
Chlorhexidine	0.500
Methylparaben	0.060
Propylparaben	0.020
Colouring agent	0.300
Water	Balance

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Biphasic mouthwash1. Cationic phase (containing $\text{SrCl}_2 \cdot 6\text{H}_2\text{O}$)

<u>Ingredient</u>	<u>% by weight</u>
$\text{SrCl}_2 \cdot 6\text{H}_2\text{O}$	10.000
Glycerin	10.000
Ethanol (190 proof, USP)	7.500
Flavour	0.500
Sodium saccharin	0.100
Chlorhexidine	0.500
Methylparaben	0.060
Propylparaben	0.020
Colouring agent	0.300
Water	Balance

2. Anionic phase

NaPO_4	0.200
Glycerin	10.000
Ethanol (190 proof, USP)	7.500
Flavour	0.500
Sodium saccharin	0.100
Chlorhexidine	0.500
Methylparaben	0.060
Propylparaben	0.020
Colouring agent	0.300
Water	Balance

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Monophasic toothpaste

<u>Ingredients</u>	<u>% by weight</u>
SrCl ₂ .6H ₂ O or CaCl ₂ .2H ₂ O	5.000
NaFPO ₃	0.500
Abrasive (precipitated silica gel)	20.000
Sorbitol (30% in H ₂ O)	20.000
Glycerin	10.000
Hydroxyethylcellulose	1.000
Sodium alkyl sulfate (28% in H ₂ O)	4.000
Saccharin	0.300
Titanium dioxide	0.500
Chlorhexidine	0.500
Flavour	1.000
Methylparaben	0.060
Propylparaben	0.020
Colour	0.700
Water	Balance

Monophasic mouthwash

<u>Ingredients</u>	<u>% by weight</u>
SrCl ₂ .6H ₂ O or CaCl ₂ .2H ₂ O	5.000
NaFPO ₃	0.500
Glycerin	10.000
Ethanol (190 proof, USP)	7.500
Flavour	0.500
Chlorhexidine	0.500
Sodium Saccharin	0.100
Methylparaben	0.060
Propylparaben	0.020
Colouring agent	0.300
Water	Balance

SUBSTITUTE SHEET

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CLAIMS

1. A system for preparing a desensitizing composition, said system comprising a source of a first ionic species and a source of a second ionic species, both sources being in physiologically acceptable form and said sources being segregated from each other, said first ionic species being selected from calcium and/or strontium ions and said second ionic species being selected from anions which combine with the first ionic species to form a salt whose solubility is less than 10 mg in 100 ml of cold water.
2. A system according to Claim 1 wherein said first and second ionic species are provided in their respective sources in concentrations such that upon mixing particles of a size suitable for occluding the tubules are formed in the tubules in a suitably short time allowing particle formation to occur before the first and second ionic species diffuse out.
3. A system, according to Claim 1 or Claim 2 wherein the calcium and/or strontium containing source is maintained at a pH of between about 3 and about 7
4. A system, according to Claim 3 wherein the calcium and/or strontium containing source is maintained at a pH of between about 5 and about 7
5. A system, according to any preceding claim wherein the concentration of the calcium and/or strontium compound is such that in the final composition it comprises between 0.1 and 20 weight per cent of the final composition (exclusive of the prescribed anion-containing composition).
6. A system, according to Claim 5 wherein the concentration of the calcium and/or strontium compound is such that in the final composition it comprises between 1 and 10 weight per cent of the final composition (exclusive of the prescribed anion-containing composition).

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7. A system, according to any preceding claim wherein the concentration of the anion-containing composition is such that the concentration in the final composition is between 0.01 and 5 (exclusive of the calcium and/or strontium-containing phase).
8. A system, according to Claim 7 wherein the concentration of the anion-containing composition is such that the concentration in the final composition is between 0.1 and 3 weight percent (exclusive of the calcium and/or strontium-containing phase).
9. A system according to any preceding claim wherein said second source of ions contains at least one anion selected from fluoride, orthophosphate, pyrophosphate, metaphosphate, carbonate and oxalate.
10. A system according to any preceding claim wherein the sources of the strontium and/or calcium ions and the anion are each maintained in a viscous aqueous medium such as in the form of a gel or a paste.
11. A densensitising composition comprising a physiologically acceptable source of strontium and/or calcium ions and a physiologically acceptable source of a suitable anion, the anions being bound in a form such that the sources are unreactive with each other at ambient conditions but upon reaction with oral liquids such as saliva a precipitate of a salt or other compound of the anion and cation is formed.
12. A package which houses a dental densensitising composition which includes a physiologically acceptable source of strontium and/or calcium ions and a physiologically acceptable source of anion as claimed in Claim 1, wherein the two sources are maintained separate from each other and are not admixed until application to the teeth is desired.

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13. A package according to Claim 12 which includes compartments, one for housing the calcium and/or strontium ions in the absence of anion, and the other for housing the specified anion in the absence of calcium and/or strontium ions.

14. The use of a physiologically acceptable source of cations to produce industrially a kit or system for the treatment of teeth in a combination therapy involving the application of said cations and anions which will combine with the chosen cations to produce a precipitate having a solubility of less than 10 mg in 100 ml of cold water, using separate compositions containing respectively said cations and said anions.

15. The use of a physiologically acceptable source of anions to produce industrially a kit or system for the treatment of teeth in a combination therapy involving the application of said anion and cations selected from calcium and/or strontium ions which will combine with the chosen anion to produce a precipitate having a solubility of less than 10 mg per 100 ml of cold water using separate compositions containing respectively said anions and said cations.

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FIG. 1

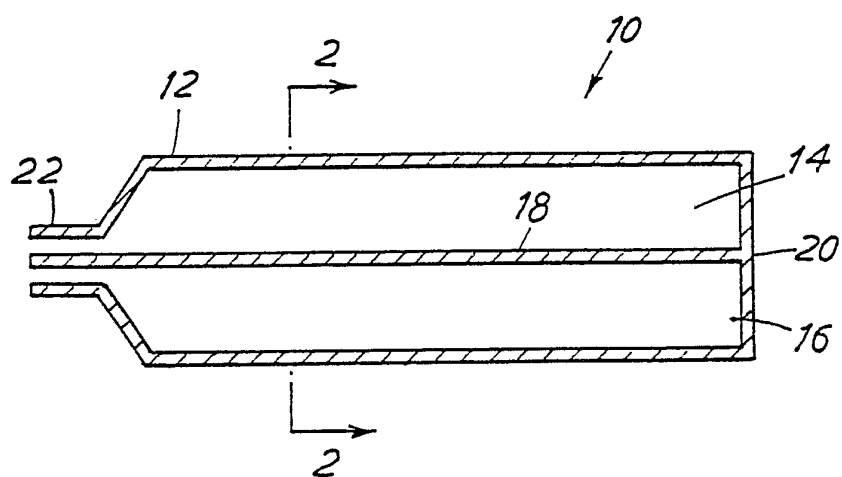
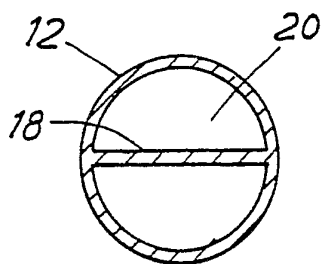


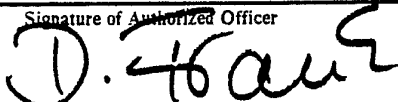
FIG. 2



INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 91/01616

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) ⁶		
According to International Patent Classification (IPC) or to both National Classification and IPC Int.Cl.5 A 61 K 7/16 A 61 K 7/18		
II. FIELDS SEARCHED		
Minimum Documentation Searched ⁷		
Classification System	Classification Symbols	
Int.Cl.5	A 61 K	
Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched ⁸		
III. DOCUMENTS CONSIDERED TO BE RELEVANT⁹		
Category ¹⁰	Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages ¹²	Relevant to Claim No. ¹³
X,P	WO,A,9010435 (AMERICAN DENTAL ASSOCIATION HEALTH FOUNDATION) 20 September 1990, see the whole document ---	1,5-10, 12-15
X	US,A,4080440 (DIGIULIO et al.) 21 March 1978, see the whole document ---	1-10,12 ,14-15
X	FR,A,2329292 (NATIONAL RESEARCH DEVELOPMENT CORPORATION) 27 May 1977, see the whole document ---	1-10,12 ,14-15
X	EP,A,0080253 (SCHOLE) 1 June 1983, see examples ---	11
X	EP,A,0263638 (UNILEVER) 13 April 1988, see the whole document --- -/-	12-13
<div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <p>¹⁰ Special categories of cited documents: ¹⁰</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation for other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> </div> <div style="width: 45%;"> <p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step</p> <p>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.</p> <p>"&" document member of the same patent family</p> </div> </div>		
IV. CERTIFICATION		
Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report	
21-10-1991	26. 11. 91	
International Searching Authority	Signature of Authorized Officer	
EUROPEAN PATENT OFFICE		

III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)		
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X	WO,A,8702890 (NEIRINCKX) 21 May 1987, see the whole document (cited in the application) -----	12-13

**ANNEX TO THE INTERNATIONAL SEARCH REPORT
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EP 9101616

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This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on 11/11/91
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