(12) STANDARD PATENT (11) Application No. **AU 2013329081 B2**
(19) AUSTRALIAN PATENT OFFICE

(54) Title
Remineralizing and desensitizing compositions, treatments and methods of manufacture

(51) International Patent Classification(s)
A61K 8/02 (2006.01) ***A61K 8/97*** (2006.01)
A61K 8/18 (2006.01) ***A61K 9/107*** (2006.01)
A61K 8/21 (2006.01) ***A61K 9/68*** (2006.01)
A61K 8/365 (2006.01) ***A61Q 11/00*** (2006.01)
A61K 8/55 (2006.01)

(21) Application No: **2013329081** (22) Date of Filing: **2013.10.11**

(87) WIPO No: **WO14/059249**

(30) Priority Data

(31) Number	(32) Date	(33) Country
13/651,044	**2012.10.12**	**US**

(43) Publication Date: **2014.04.17**
(44) Accepted Journal Date: **2018.03.29**

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(56) Related Art
US 20050196440 A1

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
17 April 2014 (17.04.2014)

WIPO | PCT

(10) International Publication Number
WO 2014/059249 A3

(51) International Patent Classification:
A61K 8/02 (2006.01)

(21) International Application Number:
PCT/US2013/064504

(22) International Filing Date:
11 October 2013 (11.10.2013)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
13/651,044 12 October 2012 (12.10.2012) US

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report (Art. 21(3))*

[Continued on next page]

(54) Title: REMINERALIZING AND DESENSITIZING COMPOSITIONS, TREATMENTS AND METHODS OF MANUFACTURE

Figure 10

(57) Abstract: Improved remineralizing and desensitizing compositions containing remineralizing ingredients in aqueous-free emulsions that, in the presence of saliva, form mucoadhesive gels substantive to tooth surfaces; wherein the gels are dissolved by saliva gradually releasing remineralizing ingredients onto tooth surfaces, treatments with these compositions and methods of manufacture.

WO 2014/059249 A3

WO 2014/059249 A3

(88) Date of publication of the international search report:
10 July 2014

REMINERALIZING AND DESENSITIZING COMPOSITIONS, TREATMENTS AND METHODS OF MANUFACTURE

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention is directed to an advance in remineralizing and desensitizing compositions, whereby the remineralizing and desensitizing ingredients are substantive to tooth surfaces, thereby extending the remineralizing or desensitizing process and corresponding remineralizing or desensitizing effectiveness. Key remineralizing and desensitizing ingredients include: various fluorides, amorphous calcium phosphate (ACPF) mixtures, bioglass (NovaMin®), tricalcium phosphate fluoride mixtures, etc.

2. Description of the Related Art

ACPF remineralizing/desensitizing compositions and their remineralizing/desensitizing effects are a preferred embodiment of the present invention. ACPF mixtures are presently marketed under the ENAMEL PRO® brand.

Remineralizing/desensitizing compositions marketed commercially that are useful in the present invention include: ACPF mixtures, bioglass compositions marketed under the trademark, NovaMin®; tricalcium phosphate fluoride mixtures marketed under the trademark, Clinpro™; various fluoride compositions marketed under trademarks including: GELKAM®, Prevident®, Periogard®, etc.

“Washout” of remineralizing/desensitizing ingredients from tooth surfaces by saliva flow, eventually controls the effective residence time of various commercial, remineralizing/ desensitizing ingredients on tooth surfaces, controlling the remineralizing/desensitizing effectiveness of the various remineralizing/desensitizing ingredients presently marketed and/or described in the prior art. To improve remineralizing/desensitizing effectiveness, commercial, professionally prescribed, fluoride remineralizing/desensitizing compositions resort to high levels of fluoride, i.e. 5000 ppm for Rx toothpastes, gels and rinses and to approximately 19,000 ppm fluoride for “in-chair” professionally applied varnishes. In contrast, standard OTC remineralizing/desensitizing toothpastes, etc., contain up to 1500 ppm fluoride under the FDA’s Fluoride Monograph.

There is a need to improve remineralizing/desensitizing effectiveness for professional oral care treatments and for OTC products for patient use, while reducing the risk associated with exposure to high fluoride levels. For the balance of this specification, the term “remineralizing” is used to describe both “remineralizing and desensitizing” treatments.

OBJECTS OF THE PRESENT INVENTION

An object of the present invention is to improve the remineralizing effectiveness of various remineralizing ingredients including: ACPF mixtures, bioglass, tricalcium phosphate, fluoride mixtures and various

fluorides in: gels, prophy pastes, rinses, chewing gums, interproximal devices, etc.

Another object of the present invention is to extend the residence time on tooth surfaces of various remineralizing ingredients used in various OTC and professional, remineralizing procedures.

A further object of the invention is to improve professional oral care “in-chair” remineralizing procedures.

Yet another object of the invention is to improve remineralizing of children’s teeth, while reducing the level of fluoride required for such remineralizing.

Yet still another object of the invention is to reduce the level of fluoride required to effect remineralization of tooth surfaces by extending the residence time of the remineralizing ingredients on tooth surfaces.

Still another object of the invention is to extend the residence time on tooth surfaces of various remineralizing ingredients, while also controlling the rate of release of various remineralizing ingredients onto tooth surfaces.

A still further object of the invention is to dispense remineralizing ingredients on to tooth surfaces in an aqueous-free emulsion such that, when they come in contact with saliva, these ingredients form mucoadhesive gels substantive to tooth surfaces; wherein the mucoadhesive gels are subsequently capable of being

solubilized by saliva flow, thereby extending the duration of the remineralizing treatment.

The remineralizing compositions and the treatments of the present invention, as detailed below, are responsive to the objects of the invention.

SUMMARY OF THE INVENTION

A first aspect of the invention provides for a remineralizing and desensitizing composition, comprising an aqueous-free emulsion comprising polydimethylsiloxane as the discontinuous phase and nonionic poloxamer surfactants as the continuous phase containing remineralizing and desensitizing ingredients of amorphous calcium phosphate fluoride combinations, wherein the amorphous calcium phosphate fluoride combination is a combination of calcium gluconate, calcium lactate gluconate, disodium hydrogen phosphate, and fluoride; wherein the pH of said amorphous calcium phosphate fluoride combinations release onto tooth surfaces is adjusted by the addition of pH control compositions selected from the group consisting of: citric acid, ascorbic acid, phosphoric acid, maleic acid and combinations thereof; and a saliva flow enhancer selected from the group consisting of Jambu resin, spilanthes extract, spilanthol, and combinations thereof;

wherein said aqueous-free emulsion is present between 5% and 26.7% weight, calcium gluconate between 2.5% and 7.5% weight, calcium lactate gluconate between 0.0873% and 2.62%, disodium hydrogen between 0.5% and 1.5% weight, and a fluoride between 0.05% and 0.138% weight; and wherein said composition comprises a substantivity enhancer selected from the group consisting of: poloxamers, carboxymethyl cellulose, carboxypolymethylene, monoalkyl esters of poly(methyl vinyl ether/maleic acid), carrageenan gum, tragancath gum, xanthan gum, guar gum, and combinations thereof, which is present between 0.1% and 0.6% weight; and

wherein said composition forms a mucoadhesive gel, upon contact with saliva, that is substantive to a tooth surface; and wherein said mucoadhesive gels are slowly solubilized upon ongoing contact with saliva, continuously releasing said remineralizing and desensitizing ingredients onto tooth surfaces to effect extended remineralization and desensitization of said tooth surfaces, with a minimum of saliva “wash-out” of said remineralizing and desensitizing ingredients.

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A second aspect of the invention provides for remineralizing and desensitizing composition that is substantive to a tooth surface and that extends the duration of remineralizing and desensitizing treatments comprising:

an aqueous-free emulsion comprising polydimethylsiloxane as the discontinuous phase and nonionic poloxamer surfactants as the continuous phase and containing therein amorphous calcium phosphate fluoride as a remineralizing and desensitizing ingredient, wherein said amorphous calcium phosphate fluoride combination is a mixture of: calcium gluconate, calcium lactate gluconate, disodium hydrogen phosphate, and a fluoride component; the composition further comprising a saliva flow enhancer selected from the group consisting of: Jambu resin, spilanthes extract, spilanthol, and combinations thereof, and a substantivity enhancer selected from the group consisting of: poloxamers, carboxymethyl cellulose, carboxypolymethylene, monoalkyl esters of poly(methyl vinyl ether/maleic acid), carrageenan gum, tragacanth gum, xanthan gum, guar gum, and combinations thereof; said aqueous-free emulsion is present between 5% and 26.7% weight, calcium gluconate between 2.5% and 7.5% weight, calcium lactate glucontate between 0.0873% and 2.62% weight, disodium hydrogen between 0.5% and 1.5% weight, and a fluoride between 0.05% and 0.138% weight; wherein:

said aqueous-free emulsion, in the presence of saliva, forms a mucoadhesive gel substantive to said tooth surfaces,

said substantive, mucoadhesive gel gradually dissolves in the presence of saliva, releasing onto said tooth surfaces, said remineralizing and desensitizing ingredients, wherein the pH of said amorphous calcium phosphate fluoride combinations released onto tooth surfaces is adjusted by the addition of pH control compositions selected from the group consisting of: citric acid, ascorbic acid, phosphoric acid, malic acid, and combinations thereof; and

said slowly released remineralizing ingredients continue to remineralize said tooth surfaces until said substantive mucoadhesive gel is solubilized by said saliva flow, thereby extending the duration of said remineralizing and desensitizing and effecting improved remineralization and desensitization of said tooth surfaces.

The present invention is directed to improved remineralizing compositions and to more effective remineralizing treatments for demineralized tooth surfaces. Active remineralizing ingredients, useful in the compositions of the invention, include: various fluorides, various amorphous calcium, phosphate fluoride mixtures (ACPF), bioglass (NovaMin®), tricalcium phosphate, fluoride mixtures and combinations thereof.

More effective remineralizing treatments of the present invention for demineralized tooth surfaces include various self-applied treatments with dental devices, toothpastes, gels, rinses, chewing gum, lozenges, etc., containing compositions of the present invention; as well as various professional "in-chair" procedures including varnishes, gels, rinses, etc., with professional versions of the compositions of the invention.

The remineralizing compositions of the present invention and remineralizing treatments of the present invention utilize an aqueous-free emulsion containing various remineralizing ingredients, wherein the emulsion in the presence of saliva forms a mucoadhesive gel that is substantive to tooth surfaces. The substantive,

mucoadhesive gel slowly dissolves in the presence of saliva, gradually releasing remineralizing ingredients, onto tooth surfaces. This slow release of remineralizing ingredients continues until the mucoadhesive gel is eventually totally solubilized by saliva. This gradual release of remineralizing ingredients from the mucoadhesive gel minimizes the “wash-out” effect of remineralizing ingredients characteristic of commercial remineralizing products and associated commercial treatments presently available.

The resultant “extended” remineralizing feature of the compositions and treatments of the present invention represent a major advance in effective remineralizing, along with reduced risk associated with lower levels of fluoride, required to effect remineralization.

ACP/aqueous-free emulsion compositions and ACPF/aqueous-free emulsion compositions are preferred embodiments of the present invention.

BRIEF DESCRIPTION OF THE DRAWINGS

The substantivity of the aqueous-free emulsion containing active ingredient, in the presence of water, is demonstrated visually by the Drawings included herein, where:

Figures 1 through 8 are photographs of three separate microscope slides, each coated with a different remineralizing toothpaste. All three slides are submersed in separate beakers containing water. The

photographs indicate various levels of substantivity of the three toothpastes at various time periods.

Figures 9 through 11 are photographs of a microscope slide coated with an aqueous-free emulsion coating showing conversion of a mucoadhesive gel upon the addition of water.

DETAILED DESCRIPTION OF THE PRESENTLY PREFERRED EMBODIMENTS

Aqueous-free emulsions of the present invention that serve as carriers for various remineralizing ingredients are characterized by their ability, in the presence of saliva, to form mucoadhesive gels which are substantive to tooth surfaces. These substantive, mucoadhesive gels of the present invention are further characterized by their ability to: (a) gradually dissolve when exposed to saliva flow, and (b) gradually release various remineralizing ingredients onto tooth surfaces. This gradual dissolution feature of mucoadhesive gels of the present invention minimizes saliva “wash-out” of remineralizing ingredients by effecting a gradual slow release of remineralizing ingredients onto tooth surfaces. The substantive, mucoadhesive gels of the present invention extend the duration of remineralizing of tooth surfaces under treatment; thereby enhancing the effectiveness of various remineralizing treatments of the present invention, while reducing the level of fluoride required to achieve effective remineralization.

All of the references cited herein, are hereby, in their entirety, incorporated by reference into the present invention.

The Role of ACPF Mixtures in Remineralizing Tooth Surfaces

The remineralizing properties of the preferred amorphous calcium phosphate fluoride mixtures (ACPF) of the present invention are described: by Ming Tung in U.S. Patents: 5,037,639; 5,268,167; 5,427,768; 5,437,857; 5,460,803; 5,562,895; by Tung in the American Dental Association Foundation publication, "ACP Technology,"; by Schemahorn, et. al., in The Journal of Clinical Dentistry Vol. XXII: No 2. 51-54, 2011; and by the 19 references cited by Schemahorn, et. al.

In addition, amorphous calcium phosphate is described by Wikipedia as follows:

> "Amorphous calcium phosphate (ACP) is a substance used as a dental treatment. Calcium and phosphate are natural building blocks of teeth, and when present in insufficient amounts, there can be sensitivity after procedures such as dental bleaching or professional dental cleansing. Amorphous calcium phosphate will help in restoring the necessary mineral balance in the mouth in an easy and efficient way.
>
> "ACP technology using a two-phase delivery system that prevents the calcium and phosphate from reacting was developed by Ming S. Tung at the American Dental Research Association's Paffenbarger Research Center. It was first used in a toothpaste called Enamelon in 1999, but it failed commercially. It is now found in Arm & Hammer's Enamel Care Toothpaste (introduced in 2004) as well as their Age Defying Toothpaste, Discus Dental's

Nite White bleaching gel, Discus Dental's Relief ACP sensitivity relief product, and Premier Dental's Enamel Pro polishing paste. It is also used in the Aegis product line, such as Aegis® Pit and Fissure Sealant with ACP, produced by the Harry J. Bosworth Company for use by dental professionals. Other Aegis Products include: Aegis® Orthodontic Adhesive with ACP, Aegis® Liner with ACP, Aegis® V with ACP and Aegis® Crown and Bridge with ACP."

According to Ming Tung, after the ACPF salts in the aqueous-free emulsions are dissolved in saliva, they precipitate and hydrolyze to tooth mineral as follows: In an acidic environment, the following reactions occur rapidly; leading to remineralization of tooth surfaces that have been physically cleaned:

The Ca^{2+} and X^{2+} $(HPO_4)^{2-}$ $+F^-$ ions precipitate as CaF_2 Ca_9 X $(PO_4)_6$ F_2 (ACXPF).

Subsequent hydrolysis of this precipitate releases fluoridated tooth mineral:

$$Ca_{10}(PO_4)_6\ F_2 + F^- + (H_{1.5}PO_4)^{1.5-} + OH + X^{24}$$

Preferred ACPF, Aqueous-free emulsions of the present invention, contain:

calcium gluconate,
calcium lactate, gluconate,
disodium hydrogen phosphate,
sodium fluoride, and
citric acid, or ascorbyl palmitate.

The aqueous-free emulsions of the present invention hold the various remineralizing salts in suspension without the salts reacting. When this aqueous-free emulsion is exposed to saliva, it forms a mucoadhesive gel that is substantive to tooth surfaces. This mucoadhesive gel continues to hold the various remineralizing ingredients without the ingredients reacting.

Eventually, this mucoadhesive gel is dissolved by saliva, releasing the unreacted ACPF components onto the hydroxyapatite. The ACPF components penetrate the hydroxyapatite, subsequently forming amorphous calcium phosphate fluoride precipitates within the hydroxyapatite.

Remineralizing, functional, aqueous-free emulsions of the present invention contain stable cations and stable anions, suitable for subsequently reacting to remineralize dental enamel; wherein:

(1) said aqueous-free emulsion inhibits premature reaction of the cations with the anions;

(2) the cations and anions are introduced onto tooth surfaces via saliva soluble, mucoadhesive gels that are substantive to: hydroxyapatite, dentin, biofilm, pellicle, soft tissue, etc.;

(3) the cations and anions are gradually released onto the hydroxyapatite as the saliva soluble, mucoadhesive gels undergo dissolution at rates generally controlled by saliva flow;

(4) local saliva flow can be further controlled by saliva enhancers such as spilanthes extract,

which are introduced onto tooth surfaces from said aqueous-free emulsion;

(5) local pH environment for said dissolving gels is controlled, in part, by pH controlling compositions, such as: ascorbyl palmitate, citric acid, etc., present in said aqueous-free emulsion, where the pH controlling composition also assists in substantivity of the various cations and anions released onto tooth surfaces upon dissolution of said mucoadhesive gels;

(6) said saliva soluble gel controls the rate of release of cations onto tooth surfaces, thereby controlling diffusion of said cations into demineralized subsurfaces and/or into dentinal tubules;

(7) said saliva soluble gel also controls rate of release of anions onto tooth surfaces, thereby controlling diffusion of said anions into demineralized subsurfaces and/or into exposed tubules;

(8) said solubilized cations and anions, after diffusing into demineralized subsurfaces and/or into exposed tubules: react and precipitate in an amorphous state remineralizing hydroxyapatite;

(9) said aqueous-free emulsion comprises polydimethylsiloxane, at various molecular weights emulsified in nonionic surfactants comprised of copolymers comprised of polyoxypropylene and polyoxyethylene that form mucoadhesive gels in the presence of saliva; and

(10) said remineralizing, functional, aqueous-free emulsions can be dispensed via: dental tape, dental floss, toothpaste, prophy paste, fluoride varnishes, fluoride gels, dry mouth gels and combinations thereof.

For purposes of the present invention, saliva soluble, aquous-free emulsions ingredients include those emulsions that are comprised of polydimethylsiloxane in a nonionic surfactant, as described in the following U.S. Patents. 5,032,387; 5,098,711; 5,538,667 and 5,651,959; all of which are hereby incorporated by reference. Only those aqueous-free emulsions described in the referenced U.S. Patents that form mucoadhesive gels substantive to tooth surfaces are useful for purposes of the present invention.

Preferred nonionic surfactants of the present invention capable of forming mucoadhesive gels in the presence of saliva, are selected from the group consisting of: poloxamer 237, poloxamer 338, poloxamer 407 and combinations thereof.

Preferred aqueous-free, saliva soluble emulsions for use in the remineralizing compositions of the present invention include emulsions of polydimethylsiloxane (PDMS) at viscosities ranging from between about 1500 cs and about 2.5 million cs. Particularly preferred, aqueous-free emulsions include as the discontinuous phase PDMS at viscosities between 10,500 cs and 2.5 million cs with those nonionic surfactants described in detail in U.S. 5,651,959 that form mucoadhesive gels in the presence of saliva, as the continuous phase.

Preferred polydimethylsiloxanes are selected from the group consisting of polydimethylsiloxane: at 1500 cs, at 12,500 cs, at 100,000 cs, at 250,000 cs, at 500,000 cs, at 750,000 cs, at 1.5 million cs, at 2.2 million cs, at 2.5 million cs and combinations thereof.

Preferred application means for the remineralizing compositions of the present invention include: oral gels, oral ointments, oral pastes, oral varnishes, toothpastes, oral liquids, lozenges, chewing gums and various interproximal devices coated with said remineralizing compositions.

The present invention is further described and illustrated in examples 1 through 29, which describe certain embodiments of the invention, while also suggesting other uses for the invention.

EXAMPLES 1 to 9

PROPHY TAPE® with ULTRAMULSION® & ACPF

Example 1

ACPF PROPHY TAPE®

A 2 gallon stainless steel vessel was fitted with an overhead stirrer and place on a hotplate. An aqueous-free emulsion comprising poloxamer 407/polydimethylsiloxane (12,500 cs) 90:10; 945.63 gm and 1200 gm of poloxamer 407 were placed in the vessel and melted while stirring. The temperature rose to 90 degrees Centigrade and the following ingredients were added: Pluracare L-1220, 120 gm; stearyl alcohol, 450.8 gm; microwax ML445, 267.6 gm; and PEG 8000, 388 gm, were added to the molten aqueous-free emulsion. A homogenizer was placed in the vessel and emulsification resulted

from 10 minutes of action. The following ACPF ingredients were then added with stirring: Calcium gluconate, 240 gm; Calcium lactate gluconate, 84 gm; disodium hydrogen phosphate, 48 gm; sodium fluoride, 4.4 gm; propyl gallate, 4 gm; sodium saccharin, 96 gm; EDTA, 8 gm; flavor, 104 gm; and citric acid, 40 gm. The emulsified tape coating batter was then dispensed into the tape coating tank. Compression coating of ultra-high-molecular-weight polyethylene dental tape at 67 mg/yard was completed to give a saliva soluble, coated, dental tape with amorphous calcium phosphate fluoride effects. The tape was overcoated with pumice at between 6 and 10 gm/yd and post-flavored via flavor transfer from a flavor reservoir.

Following the procedures set out in Example 1, PROPHY TAPE® Examples 2 through 9, as detailed in Table 1 below, were prepared. All PROPHY TAPES® were overcoated with pumice abrasive and post-flavored via flavor transfer from a flavor reservoir in a flavor-sealed package.

Table 1
ACPF PROPHY TAPE® EXAMPLES 2 through 9

ACPF Ingredients (all % by wt.)

Example #	Aqueous-free Emulsion	Gluconate Phosphate	Calcium Lactate	Disodium Hydrogen	Sodium Fluoride
2	23.81	7.5	2.62	1.5	0.09
3	26.7	5	1.74	1.0	0.05
4	11	7.5	2.62	1.5	0.138
5	5	7.5	2.62	1.5	0.138
6	11	5	1.74	1.0	0.09

7	5	5	1.74	1.0	0.09
8	11	2.5	0.873	0.5	0.05
9	5	2.5	0.873	0.5	0.05

ILLUSTRATIVE EXAMPLES 10 through 24

Examples summarized in Tables 2 through 4 below, further illustrate the broad range of improved remineralizing compositions, in various dispensing means.

All of the illustrative remineralizing Examples, set out Tables 2 through 4, are to be formulated to form mucoadhesive gels when dispensed in the presence of saliva, which mucoadhesive gels are substantive to tooth surfaces and capable of gradual dissolution upon continuous exposure to saliva.

Following the procedures in Example 1, the aqueous-free emulsion compositions can be prepared and used for coating PROPHY TAPE®, PTFE dental tape and multifilament dental floss, as detailed in Examples 10 through 14 in Table 2 below.

Table 2
Illustrative Examples 10 through 14

PROPHY TAPE®, PTFE Dental Tape, Multifilament Dental Floss

Example #	Composition of Aqueous Free Emulsion	Remineralization Ingredients (% by wt.)	Saliva Enhancement Ingredient (% by wt.)	Dispensing Means
10	PDMS(2.5mm cs)	Bioglass (7.5)	Spilanthes Extract (0.6)	Multifilament dental floss with base

	10% in poloxamer 407 at 24%			coating between 40 and 60 mg/yd
11	PDMS(2.5mm cs) 20% in poloxamer 407 at 15%	Tricalcium Phosphate (5), Sodium Fluoride (1.1)	Spilanthes Extract (0.2)	Multifilament dental floss with base coating between 50 and 70 mg/yd
12	PDMS(12,500 cs) 20% in poloxamer 407 at 25%	Stannous Fluoride (2.06)	Spilanthes Extract (0.15)	Multifilament dental floss with base coating between 50 and 70 mg/yd
13	PDMS(2.5mm cs) 10% in poloxamer 338 at 25%	Sodium mono-fluorophosphate (3.78)	Spilanthes Extract (0.4)	Multifilament dental floss with base coating between 55 and 75 mg/yd
14	PDMS(2.5mm cs) 20% in poloxmer 407 at 20%	Sodium Fluoride (1.11)	Spilanthes Extract (0.1)	Multifilament dental floss with base coating between 60 and 80 mg/yd

Following the procedure in Example 1, the remineralizing, aqueous-free emulsion compositions described in Examples 15 through 19 in Table 3 below can be prepared for use in Prophy Pastes, and various alternatives to Prophy Pastes.

Table 3
Illustrative Examples 15 through 19

Example #	Composition of Aqueous free Emulsion (% by wt.)	Remineralization Ingredients (% by wt.)	Saliva Enhancement Ingredient (% by wt.)	Dispensing Means
15	PDMS (2.5mm cs) 35% in poloxamer 407 at 1%	Bioglass (5)	Spilanthes extract (0.4)	prophy paste
16	PDMS (2.5mm cs) 10% in poloxamer 338 at 3%	Tricalcium phosphate (5) and sodium fluoride (1.1)	Spilanthes extract (0.25)	prophy paste
17	PDMS (2.5mm cs) 35% in poloxamer 407 at 1.5%	Stannous fluoride (2.1)	Spilanthes extract (0.1)	prophy paste
18	PDMS (2.5mm cs) 35% in poloxamer 407 at 1%	Sodium mono-fluorophosphate (3.79)	Spilanthes extract (0.12)	prophy paste
19	PDMS (2.5mm cs) 35% in poloxamer 338 at 1%	Sodium fluoride (1.1)	Spilanthes extract (0.3)	prophy paste

EXAMPLES 20 through 24

Following the procedures in Example 1, the aqueous-free emulsion compositions can be prepared and used for toothpaste, as detailed in Example 20 through 25 of Table 4.

Table 4
Illustrative Examples 20 through 25

Example #	Composition of Aqueous free Emulsion (% by wt.)	Remineralization Ingredients (% by wt.)	Saliva Enhancement Ingredient (% by wt.)	Dispensing Means
20	PDMS (2.5mm cs) 20% in poloxamer 407 at 3%	Bioglass (6)	Spilanthes extract (0.12)	toothpaste
21	PDMS (2.5mm cs) 10% in poloxamer 407 at 3%	Tricalcium phosphate (5) and sodium fluoride (1.1)	Spilanthes extract (0.1)	toothpaste
22	PDMS (2.5mm cs) 20% in poloxamer 338 at 2%	Stannous fluoride (2.06)	Spilanthes extract (0.2)	toothpaste
23	PDMS (2.5mm cs) 20% in poloxamer 407 at 2.5%	Sodium mono-fluorophosphate (3.79)	Spilanthes extract (0.25)	toothpaste
24	PDMS (2.5mm cs) 10% in poloxamer 338 at 2%	Sodium fluoride (1.1)	Spilanthes extract (0.1)	toothpaste
25	PDMS (2.5mm cs) 10% in poloxamer 407 at 2%	ACP (5.0)	Spilanthes extract (0.1)	Children's fluoride-free toothpaste

EXAMPLE 26

Multifilament Dental Floss with ACPF

A 3 gallon stainless steel vessel was fitted with an overhead stirrer and a hot plate. The following ingredients were added with stirring and heating to 90 degrees Centigrade: an aqueous-free emulsion (poloxamer

407, 2673.7 gm; silicone AF1500, 400 gm); sodium saccharin, 92 gm; propyl gallate, 4 gm; silica, 160 gm; sodium fluoride, 5.52 gm; calcium gluconate, 300 gm; calcium lactate gluconate, 104.8 gm; disodium hydrogenphosphate, 60 gm; flavor, 160 gm and citric acid, 40 gm. The vessel was heated and stirred for 20 minutes and the contents transferred to the dental floss applicator tank. Compression coating of the 840 texturized nylon 6,6 yarn produced a dental floss with a coating level of 84 mg/yd. Prior to flossing, the multifilament floss is stretched and released, allowing the texturized floss to expand thereby optimizing interproximal delivery of calcium, phosphate and fluoride to tooth surfaces while leaving a clean just-brushed feeling.

EXAMPLE 27

Children's Fluoride-Free Toothpaste with ACP/Aqueous-Free Emulsion

A Hobart N-50 mixer fitted with a 1 gallon stainless steel bowl was used to mix the following: PEG 400, 272 gm; an aqueous-free emulsion [poloxamer 407/polydimethyl-siloxane (90:10)], 64 gm; poloxamer 407, 80.8 gm; pluracol L-1220, 80.8 gm; Carbopol 974P, 12 gm; glycerin, 584.8 gm; xylitol powder, 48 gm; acesulfame K, 4.8 gm; titanium dioxide, 16 gm; zeodent, 80 gm; sipernat 22S, 120 gm; perlastin L, 8 gm; sucralose, 2.4 gm; flavor, 28 gm, were stirred for 5 minutes at room temperature. The contents of the bowl were heated to 80 degrees Centigrade. Calcium gluconate, 128 gm; calcium lactate gluconate, 44.8 gm and disodium hydrogenphosphate, 25.6 gm, were then added. After stirring for 10 minutes, the content of the

one gallon vessel was transferred to 1.5 oz tubes. Application of 1.5 gram of the toothpaste to the oral mucosa with brushing delivers amorphous calcium phosphate, remineralizing effects; relying on mucoadhesive properties of the gel formed on tooth surfaces in the presence of saliva.

EXAMPLE 28

Adult Toothpaste with ACPF/Aqueous-Free Emulsion

A Hobart N-50 mixer fitted with a 1 gallon stainless steel bowl was used to mix the following: PEG 400, 272.48 gm; an aqueous-free [poloxamer 407/polydimethyl-siloxane (90:10)], 24 gm; Carbopol 974P, 12 gm; glycerin, 744.96 gm; xylitol powder, 80 gm; acesulfame K, 4.8 gm; titanium dioxide, 16 gm; zeodent 113, 80 gm; sipernat 22S, 120 gm; perlastin L, 16 gm; sucralose, 2.4 gm and flavor, 28.8 gm, were stirred for 5 minutes at room temperature. The contents of the bowl were heated to 80 degrees Centigrade. Calcium gluconate, 128 gm; calcium lactate gluconate, 44.8 gm and disodium hydrogenphosphate, 25.6 gm, were then added. After stirring for 10 minutes, the content of the one gallon vessel was transferred into 2 oz tubes. Application of 2 gram of the toothpaste to the oral mucosa with brushing delivers amorphous calcium phosphate fluoride, remineralizing; relying on the mucoadhesive gel formed on tooth surfaces in the presence of saliva.

EXAMPLE 29

Comparative Substantivity of Three Toothpastes

An experiment was designed to compare the substantivity properties of three toothpastes. A separate microscope

slide was utilized as substrates for each toothpaste. A small bead of toothpaste was applied to a saliva-coated slide. The bead was leveled with a microscope clover slip to obtain a thin coating simulating the thin coat a toothbrush might apply. This procedure was repeated for each of three toothpaste samples. Each slide was immersed in 17 ml of water in a 50 ml beaker. Photographs were taken of side-by-side beakers containing each slide with the thin layer of test toothpaste submerged in water. Photographs at 0, 1, 3, 4, 5, 10, 15 and 20 minutes show the rapid loss of adhesion for the NUPRO® SENSODYNE® toothpaste at one minute and similar loss of adhesion for Clinpro™ 5000 Toothpaste after three minutes. The substantivity of the Children's ACP/ULTRAMULSION® toothpaste to the slide after 20 minutes indicates the substantivity of the mucoadhesive gel that forms in the presence of water or saliva.

The photographs at 0, 1, 3, 4, 5, 10, 15 and 20 minutes are included as Figures 1 through 8 of the Drawings.

AN AQUEOUS-FREE EMULSION OF THE INVENTION FORMS A MUCOADHESIVE GEL

A microscope slide coated with an aqueous-free emulsion of the present invention was treated with water. The photographs of the coated slide before and after application of water are included as Figs. 9 through 11 of the Drawings.

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Claims:

1. A remineralizing and desensitizing composition, comprising an aqueous-free emulsion comprising polydimethylsiloxane as the discontinuous phase and nonionic poloxamer surfactants as the continuous phase containing remineralizing and desensitizing ingredients of amorphous calcium phosphate fluoride combinations, wherein the amorphous calcium phosphate fluoride combination is a combination of calcium gluconate, calcium lactate gluconate, disodium hydrogen phosphate, and fluoride; wherein the pH of said amorphous calcium phosphate fluoride combinations release onto tooth surfaces is adjusted by the addition of pH control compositions selected from the group consisting of: citric acid, ascorbic acid, phosphoric acid, maleic acid and combinations thereof; and a saliva flow enhancer selected from the group consisting of Jambu resin, spilanthes extract, spilanthol, and combinations thereof;

wherein said aqueous-free emulsion is present between 5% and 26.7% weight, calcium gluconate between 2.5% and 7.5% weight, calcium lactate gluconate between 0.0873% and 2.62%, disodium hydrogen between 0.5% and 1.5% weight, and a fluoride between 0.05% and 0.138% weight; and wherein said composition comprises a substantivity enhancer selected from the group consisting of: poloxamers, carboxymethyl cellulose, carboxypolymethylene, monoalkyl esters of poly(methyl vinyl ether/maleic acid), carrageenan gum, tragancath gum, xanthan gum, guar gum, and combinations thereof, which is present between 0.1% and 0.6% weight; and

wherein said composition forms a mucoadhesive gel, upon contact with saliva, that is substantive to a tooth surface; and wherein said mucoadhesive gels are slowly solubilized upon ongoing contact with saliva, continuously releasing said remineralizing and desensitizing ingredients onto tooth surfaces to effect extended remineralization and desensitization of said tooth surfaces, with a minimum of saliva "wash-out" of said remineralizing and desensitizing ingredients.

2. A remineralizing and desensitizing composition that is substantive to a tooth surface and that extends the duration of remineralizing and desensitizing treatments comprising:

an aqueous-free emulsion comprising polydimethylsiloxane as the discontinuous phase and nonionic poloxamer surfactants as the continuous phase and containing therein amorphous calcium phosphate fluoride as a remineralizing and desensitizing ingredient, wherein said amorphous calcium phosphate fluoride combination is a mixture of: calcium

gluconate, calcium lactate gluconate, disodium hydrogen phosphate, and a fluoride component; the composition further comprising a saliva flow enhancer selected from the group consisting of: Jambu resin, spilanthes extract, spilanthol, and combinations thereof, and a substantivity enhancer selected from the group consisting of: poloxamers, carboxymethyl cellulose, carboxypolymethylene, monoalkyl esters of poly(methyl vinyl ether/maleic acid), carrageenan gum, tragacanth gum, xanthan gum, guar gum, and combinations thereof; said aqueous-free emulsion is present between 5% and 26.7% weight, calcium gluconate between 2.5% and 7.5% weight, calcium lactate glucontate between 0.0873% and 2.62% weight, disodium hydrogen between 0.5% and 1.5% weight, and a fluoride between 0.05% and 0.138% weight; wherein:

said aqueous-free emulsion, in the presence of saliva, forms a mucoadhesive gel substantive to said tooth surfaces,

said substantive, mucoadhesive gel gradually dissolves in the presence of saliva, releasing onto said tooth surfaces, said remineralizing and desensitizing ingredients, wherein the pH of said amorphous calcium phosphate fluoride combinations released onto tooth surfaces is adjusted by the addition of pH control compositions selected from the group consisting of: citric acid, ascorbic acid, phosphoric acid, malic acid, and combinations thereof; and

said slowly released remineralizing ingredients continue to remineralize said tooth surfaces until said substantive mucoadhesive gel is solubilized by said saliva flow, thereby extending the duration of said remineralizing and desensitizing and effecting improved remineralization and desensitization of said tooth surfaces.

3. An improved remineralizing composition according to Claims 1 or 2, wherein said polydimethylsiloxane discontinuous phase has a viscosity between about 1500 cs and about 2.5 million cs.

4. An improved remineralizing composition according to Claim 3, wherein said nonionic surfactant continuous phase comprises nonionic poloxamer surfactants that form mucoadhesive gels in the presence of saliva, wherein said gels are substantive to tooth surfaces.

5. An improved remineralizing composition according to Claim 4, wherein said nonionic surfactant is selected from the group consisting of: poloxamers, polysorbates, poloxyethylene alcohols and combinations thereof.

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6. Improved remineralizing compositions according to Claims 1 or 2, wherein dispensing means for said improved remineralizing compositions are selected from the group consisting of: interproximal devices coated with said compositions, prophy paste, varnish, gel, toothpaste, chewing gum, sealant, rinse, and combinations thereof.

Premier Dental Products Company
Whitehill Oral Technologies, Inc.

Patent Attorneys for the Applicant/Nominated Person
SPRUSON & FERGUSON

Figure 1

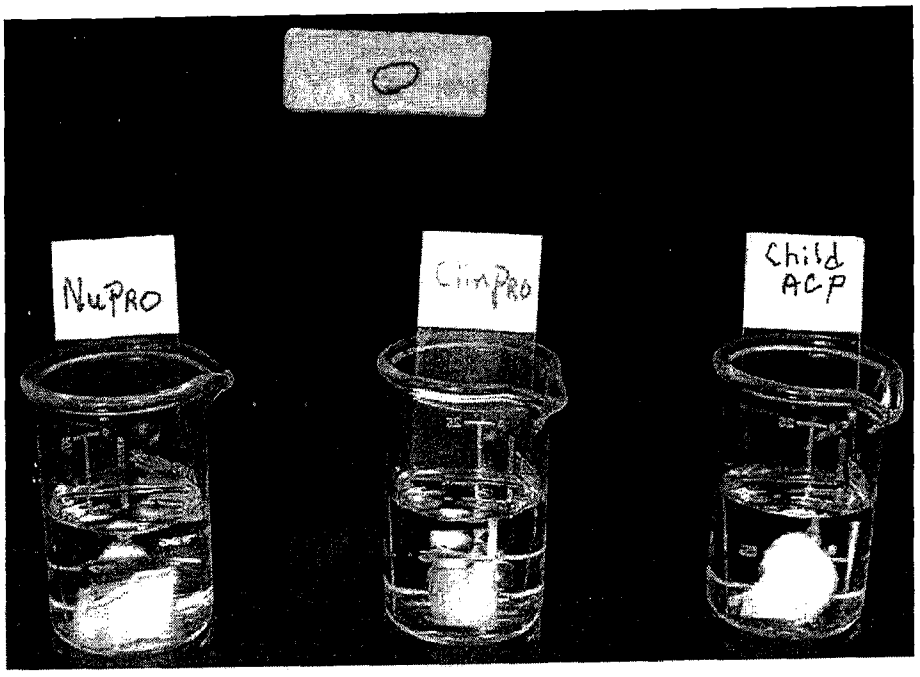


Figure 2

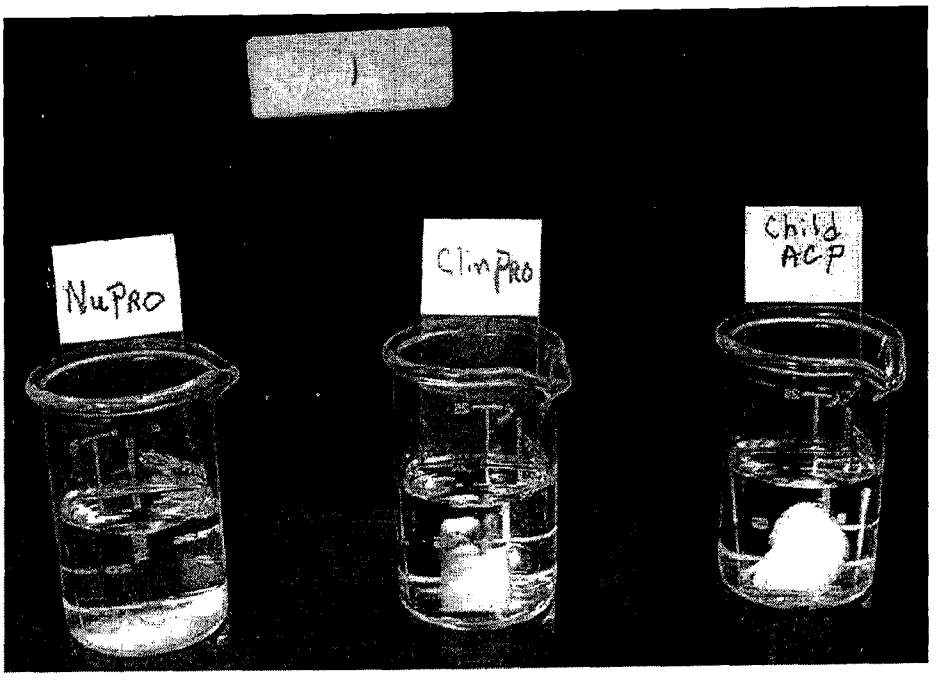


Figure 3

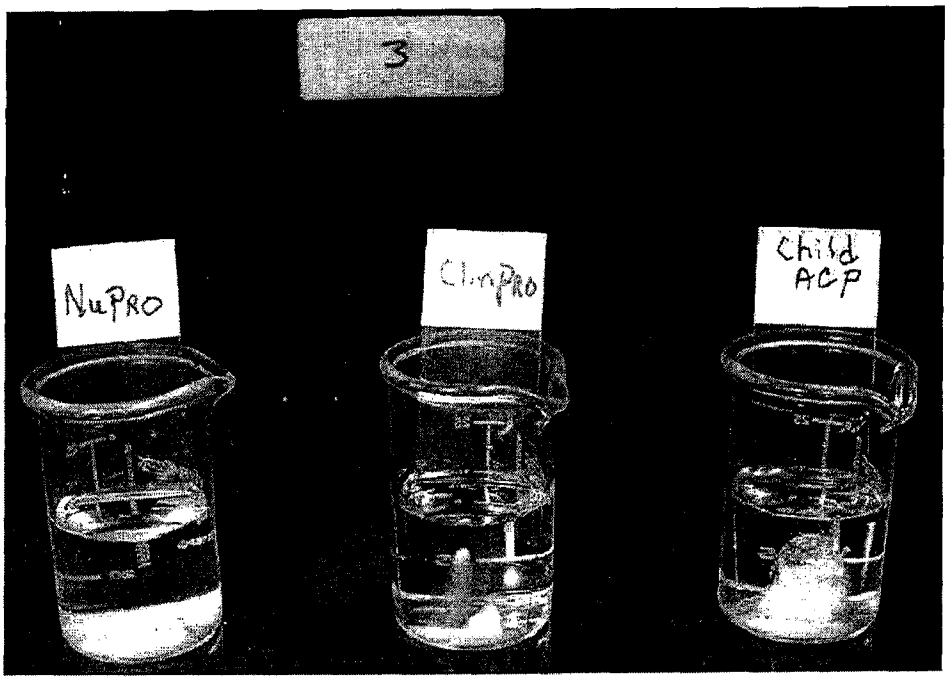


Figure 4

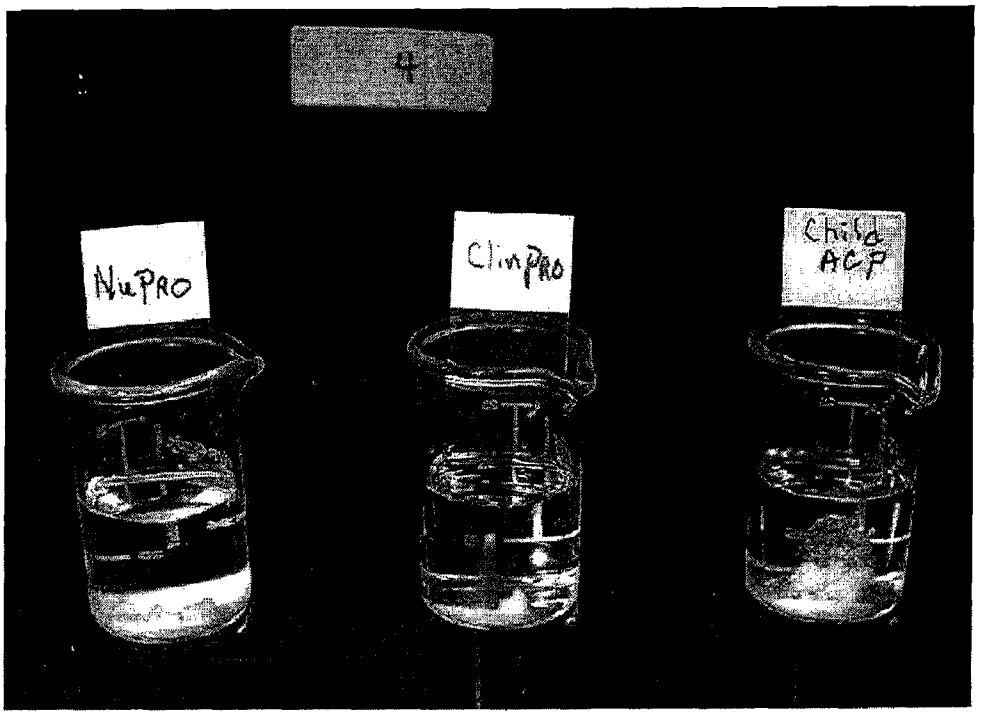


Figure 5

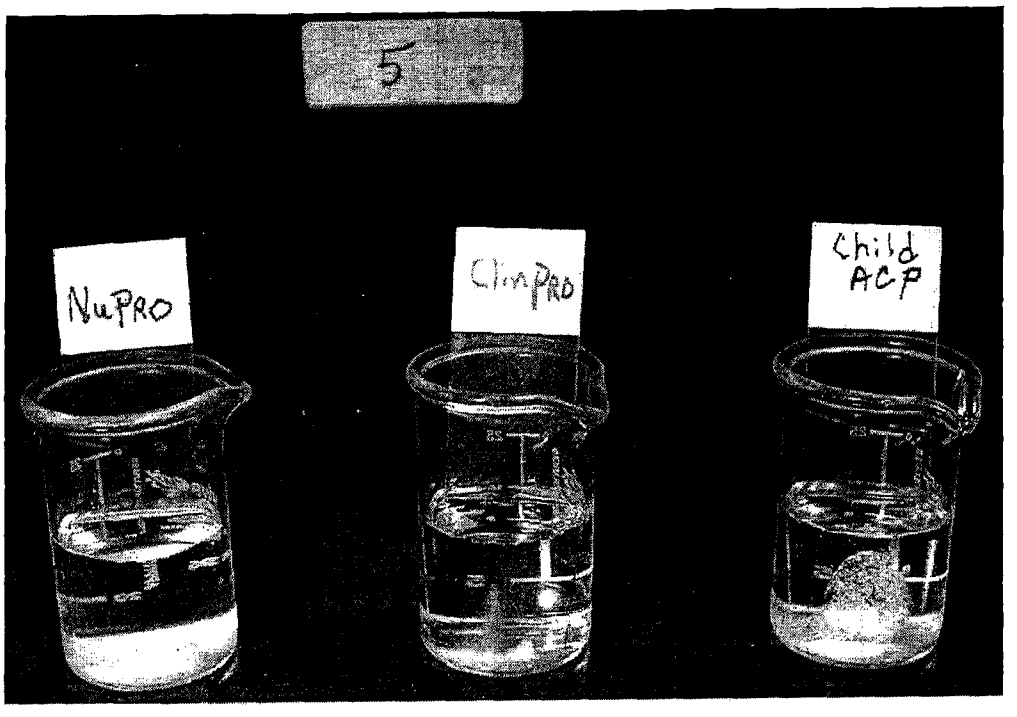


Figure 6

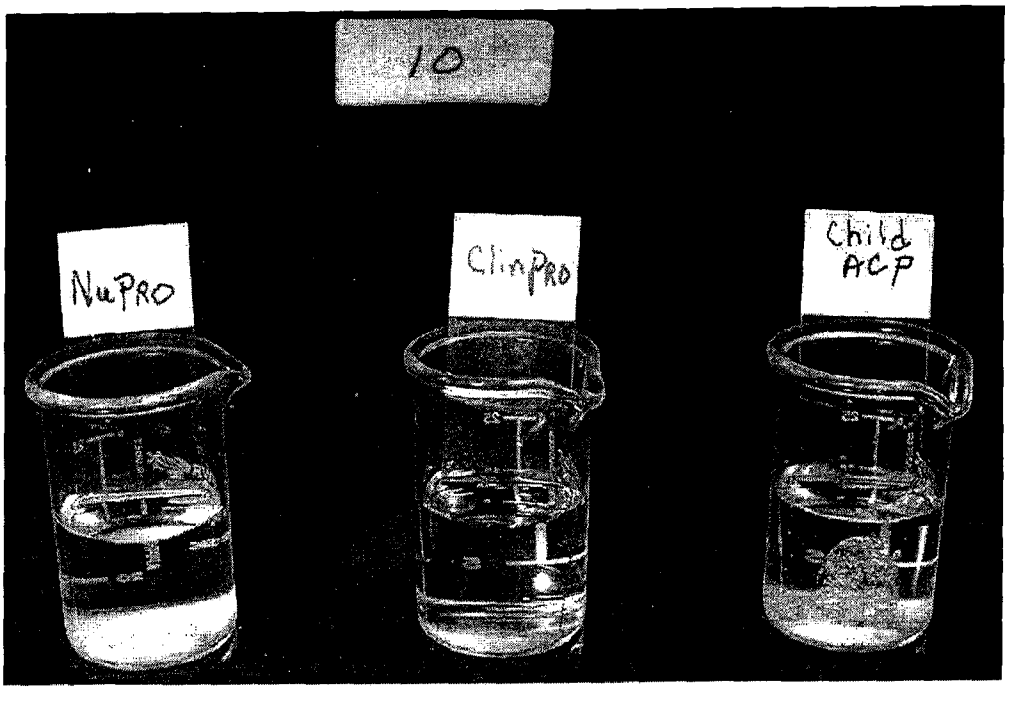


Figure 7

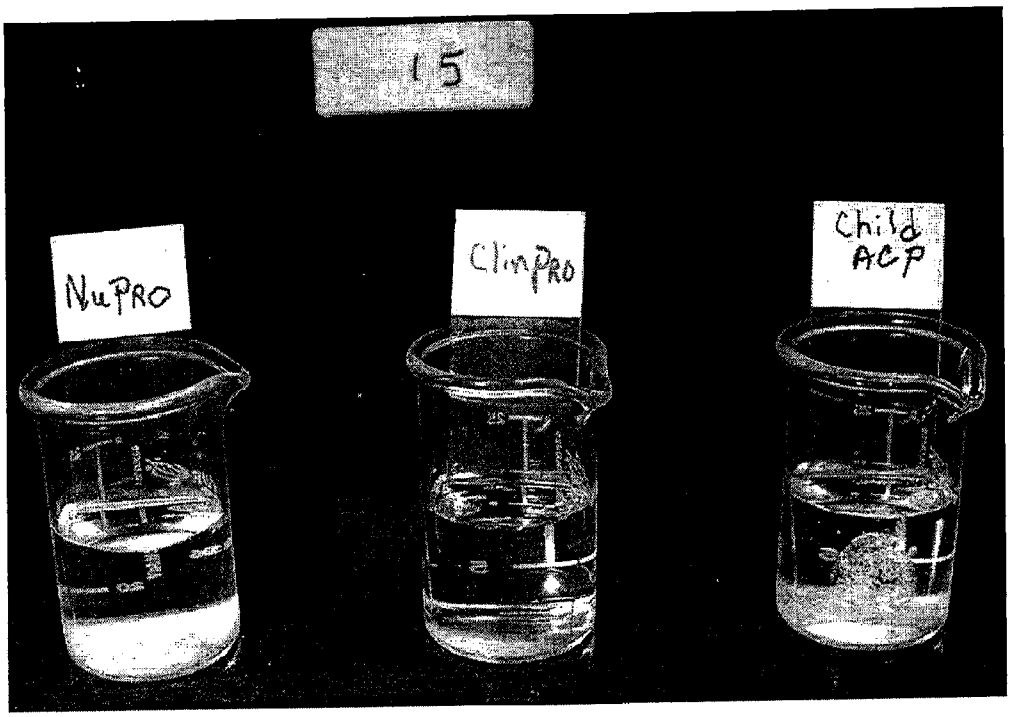


Figure 8

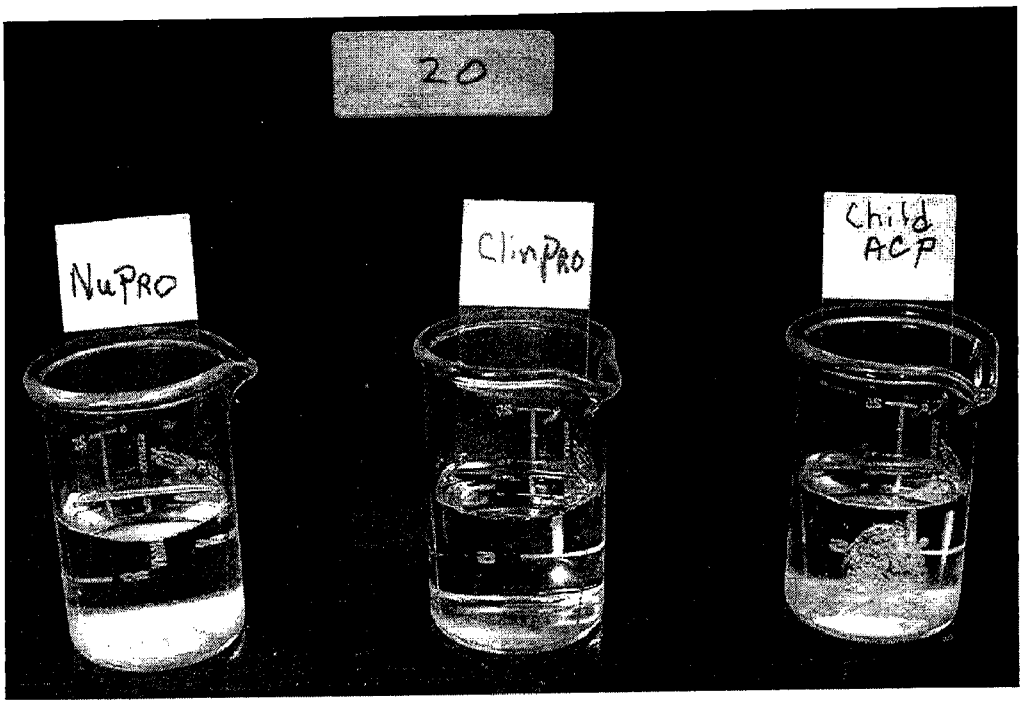
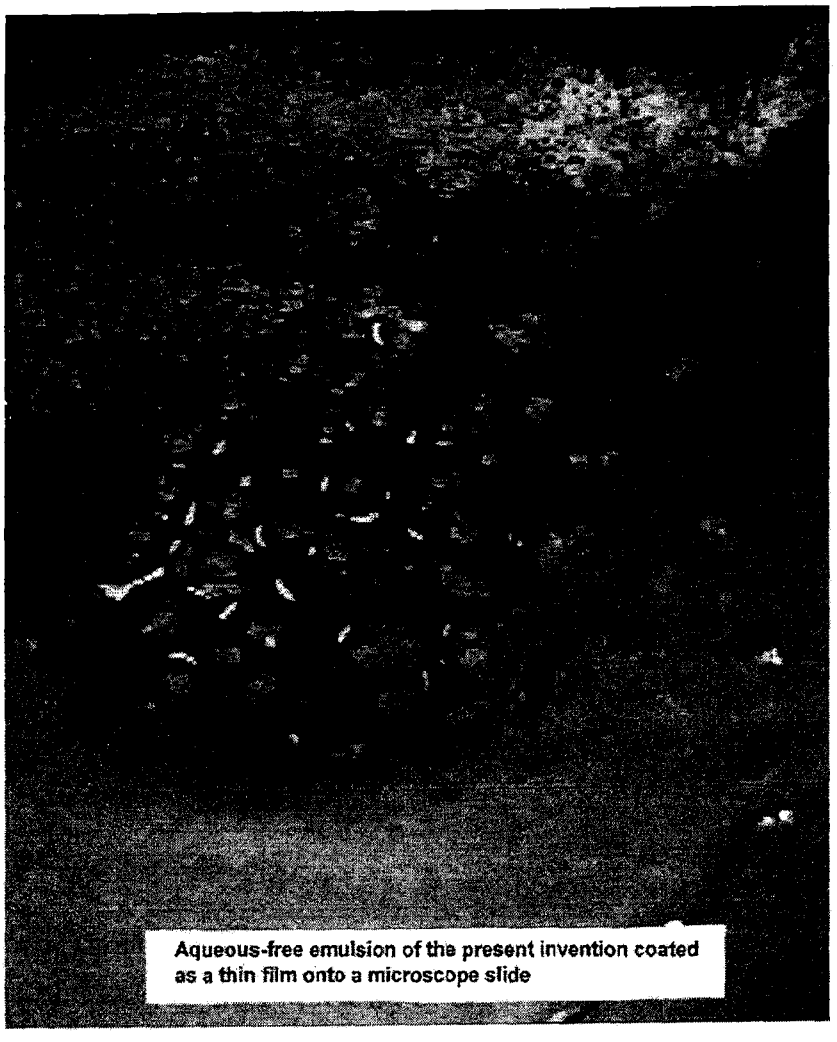


Figure 9


Aqueous-free emulsion of the present invention coated as a thin film onto a microscope slide


Aqeous-free emulsion of the present invention after exposure to water. The shiny semi-opaque interface of water and the aqueous-free emulsion indicates a gel structure

Figure 10


ENAMELON® fluoride-free, CHILDREN'S REMINERALIZING
TOOTHPASTE with ACP AND ULTRAMULSION®
after 24hrs in water when applied to a glass slide

Figure 11