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"CELLULOSE DERIVATIVES FOR GELLING AGENTS IN DENTAL CREAMS"

The present invention relates to dental cream. Sodium carboxymethyl cellulose has commonly been used as the gelling agent of commercial choice in dental creams in view of its availability and the generally satisfactory rheological properties it gives to dental creams, particularly when they are made and used in temperature climates. In tropical climates it can be subject to decomposition by cellulase.

There is an observable tendency of dental creams formulated with many grades of sodium carboxymethyl cellulose to become rough (soft lump or chunk formation) in appearance even at room temperature, particularly when subject to dynamic aging, this is extrusion of 2 cm of dental cream ribbon from a tube twice a day for 2 weeks, a condition which simulates normal use of a dental cream by one person.

Even grades of sodium carboxymethyl cellulose which do not undergo such roughening upon dynamic aging can reveal other rheological problems, for instance poor "stand-up" qualities, that is, the rapid settling of the extruded cream into a flat ribbon or thickening with the passage of time.

It is noteworthy that roughening on dynamic aging is particularly observable when the dental cream contains a compound which provides fluoride and a calcium phosphate is present as polishing material.

Thus, there is little problem when fluoride is provided from sodium monofluorophosphate or a mixture of sodium monofluorophosphate and sodium fluoride and the polishing agent is siliceous material. However, the problem is readily observable when fluoride is provided from sodium monofluorophosphate or a mixture of sodium monofluorophosphate and sodium fluoride in a dental cream containing at least about 35% by weight of a calcium phosphate polishing material such as dicalcium phosphate.

Attempts of overcome the roughening problem without having other problems such as poor "stand-up" have involved mixing different grades of sodium carboxymethyl cellulose with other gelling agents such as synthetic inorganic silicated clay (e.g. materials available under the trademarks "Laponite" and "Veegum"), thickeners such as silica thickeners available from Huber under the trademark "Zeosyl" such as Zeosyl 200 and from Rhone Poulenc as Tixosil (Registered Trade Mark) and as Tixosil 33J or available from Wacker under the identification "HDK N20", and liquid phase material such as polyethylene glycol 600. Such attempts have not been fully successful.

Hydroxyethyl cellulose has been suggested as an alternative gelling agent to sodium carboxymethyl cellulose and indeed grades of hydroxyethyl cellulose such as Natrosol (Registered Trade Mark) M have been used in commercial dental creams and grades have been set forth, for instance in U.S. Patents 3,862,307

(Natrosol G), and 3,070,510 (viscosity of 75-125 cps-Brookfield; 20°C; 2% in water) and 4,022,881 (Natrosol 250H, a high viscosity material). Such grades of hydroxyethyl cellulose, while generally satisfactory may tend to cause dental creams to undergo extensional rheology by forming a visible "tail" during container filling and upon extrusion onto a toothbrush. For instance, "stringiness" was described in U.S. Patent 4,022,881 in toothpastes containing a thickening agent mixture of 30% hydroxethyl cellulose and 70% sodium carboxymethyl cellulose. A non-stringy toothpaste containing calcium carbonate abrasive with a thickening agent mixture of 10% hydroxethyl cellulose and 90% sodium carboxymethyl cellulose was also set forth.

In accordance with aspects of the present invention a gelling agent mixture is provided which has little susceptibility to roughness upon aging and also possesses other desirable rheological properties such as good "stand up", absence of formation of a "tail" on an extruded ribbon of dental cream and good ribbon gloss. Moreover, dental cream can be readily manufactured without substantial modification of the procedures used when sodium carboxymethyl cellulose is the gelling agent.

According to the present invention a dental cream comprises about 20-75% of a polishing material, at least about half of which is hydrated alumina and about 20-80% by weight based on the weight of the dental cream of a liquid phase containing water, humectant or a mixture thereof and about 0.5-5% by weight based on the weight of the dental cream of a gelling agent consisting essentially of hydroxyethyl cellulose having a high viscosity in a range the average of which is at least about 24000 cps, determined on a Brookfield viscometer in 2% by weight water:glycerine (1:1.56) solution at 20°C with a No. 6 spindle at 20 rpm.

The gelling agent is present in the dental cream in an amount of about 0.5-5% by weight, preferably about 0.8-2%, and most preferably about 0.9-1.4%. A typical grade of hydroxyethyl cellulose effective in the practice of this aspect of the present invention is Tylose H10000P, available from Farbwerke Hoechst of Frankfurt am Main, Germany.

This invention also relates to a dental cream comprising a binary fluoride source comprising or consisting of a mixture of sodium monofluorophosphate and sodium fluoride in which about 30-40% by weight of said fluoride is from said sodium fluoride in an amount to provide about 750-2000 ppm total of ionic fluoride, about 35-75% by weight of a polishing agent consisting essentially of a calcium phosphate and a dental vehicle comprising about 20-80% by weight based on the weight of the dental cream of a liquid phase containing water, humectant or a mixture thereof and about 0.5-5% by weight based on the weight of the dental cream of a gelling agent consisting essentially of hydroxyethyl cellulose having a high viscosity of in a range the

average of which is at least about 24000 cps, determined on a Brookfield viscometer in 2% water:glycerine (1:1.56) solution at 20°C with a No. 6 spindle at 20 rpm.

Tylose H10000P and other grades of hydroxyethyl cellulose useful in the practice of the present invention have viscosities in a range the average of which is at least about 24000 cps. determined on a Brookfield viscometer at 20°C, in a water:glycerine (1:1.56) solution with a No. 6 spindle at 20 rpm. Hydroxyethyl cellulose grades of high viscosity which may be used in these aspects of the present invention are set forth in the following Table 1:

TABLE 1

SUPPLIER	HEC GRADE	VISCOSITY
Hercules	Natrosol 250 HR and 250 H	17000-31000
	Natrosol 250 HHR and 250 HH	37000-41000
Hoechst	Tylose H 10000P	20000-30000

Hydroxyethyl cellulose grades of viscosity not reaching an average of about 24000 cps, such as Hercules (Registered Trade Mark) 250 M and MR (average viscosity of 15500 cps) and Hoechst Tylose H 40000 P (viscosity of up to 23000 cps), do not provide the desired rheology when used as the only gelling agent..

Further advantages of this invention, particularly when calcium phosphate polishing agent is employed, are provided in dental creams containing a source of fluoride, for example a binary source of fluoride from sodium monofluorophosphate and sodium fluoride, and a

polishing agent including a calcium phosphate.

Rheological advantages of this invention are evident when the dental cream contains a compound which provides at least about 100 pm of fluoride, for example about 100-10000 ppm, typically about 750-2000 ppm. Compounds which provide fluoride include sodium fluoride, stannous fluoride, potassium fluoride, potassium stannous fluoride, sodium hexafluorostannate, stannous chlorofluoride and sodium monofluorophosphate. Most typically in accordance with the present invention sodium monofluorophosphate or a mixture of sodium monofluorophosphate and sodium fluoride is employed.

The dental cream typically contains sodium monofluorophosphate or a mixture of sodium monofluorophosphate and sodium fluoride in an amount to provide about 100-10000 ppm of fluoride, e.g. about 750-2000 ppm, or particularly about 1400-2000 such as about 1400-1670 ppm. A binary fluoride system of sodium monofluorophosphate and sodium fluoride is desirably used in which about 30-40% of the fluoride (e.g. about 30-35%, that is about 300-580 ppm) is provided by sodium fluoride.

Thus, in a typical dental cream, sodium monofluorophosphate is typically used in the binary system in an amount to provide about 700-1090 ppm fluoride to the dental cream in which the total amount of fluoride is about 1000-1670 ppm with about 30-35% weight to the total fluoride being provided by sodium fluoride (about 300-580 ppm). This corresponds to about 0.5-1.2% by weight of sodium monofluorophosphate and about 0.05-0.11% by weight of sodium fluoride. Preferably, the dental cream thereof contains about 1000-1500 ppm, most preferably, about 950-1000 ppm

fluoride provided by sodium monofluorophosphate and about 450-500 ppm provided by sodium fluoride.

Sodium monofluorophosphate, Na_2PO_3F, as commercially available, may vary considerably in purity. It may be used in any suitable purity provided that any impurities do not substantially adversely affect the desired properties. In general, the purity is desirably at least 80%. For best results, it should be at least 85%, and preferably at least 90% by weight of sodium monofluorophosphate with the balance being primarily impurities or by-products of manufacture such as sodium fluoride and water-soluble sodium phosphate salt. Expressed in another way, the sodium monofluorophosphate employed should have a total fluoride content of above 12%, preferably above 12.7%, a content of not more than 1.5%, preferably not more than 1.2% of free sodium fluoride; and a sodium monofluorophosphate content of at least 12%; preferably at least 12.1% all calculated as fluoride.

As indicated above, sodium fluoride in the binary mixture is a separate fluoride-containing component from sodium monofluorophosphate. About 300-580 ppm of fluoride is preferably provided to the dental cream by the sodium fluoride.

As mentioned above the dental cream contains about 20-75% by weight of a polishing agent at least about half of which is hydrated alumina. If desired, up to about half of the total polishing agent may be additional dentally acceptable polishing material such as silica, dicalcium phosphate, calcined alumina, zirconium silicate, or insoluble sodium metaphosphate. Preferably about 40-55% of polishing material, typically all hydrated alumina, is present.

The hydrated alumina employed in accordance with the present invention is preferably small in particle size, i.e. at least about 85% of the particles are smaller than 20 microns, such as that classified as gibbsite (alpha alumina trihydrate) and normally represented chemically as $Al_2O_3.3H_2O$ or $Al(OH)_3$.

The alpha alumina trihydrate may have a size in the range of about 2.6-10 microns. The alpha alumina trihydrate sold by Alcoa as C333 is a fine grade of gibbsite and is particularly highly desirable. The average particle size of C333 alumina is about 7-9 microns (Coulter-Counter). It is obtained by fine grinding of the grade of alumina trihydrate sold by Alcoa as C33. Other grades of hydrated alumina which may be employed include AF 260 and AF 230 sold by British Aluminium Company and SH 100 sold by Rhone-Poulenc.

The hydrated alumina dental cream is typically packaged in a form of container from which it can be readily extruded such as a pressure differential or mechanically operated dental cream dispenser or a lined or unlined aluminium tube or lead tube or laminated tube. The rheological properties are particularly desirable when a mechanically operated dispensing container of the type described in British Patent Application 2,070,695A, published September 9, 1981, is employed. This dispensing container comprises a dispensing mouthpiece, a tension member, a piston and operating hand control.

The disclosure of this published application is incorporated herein by reference. Pressure differential dispensing containers may be of the aerosol or vacuum type.

Hydrated alumina dental creams may contain a compound which provides fluoride or binary sources of fluoride, as described above.

Calcium phosphate dental creams typically contain about 35-75% by weight, preferably 40-55% of a dentally acceptable water-insoluble polishing material which consists essentially of a calcium phosphate, such as dicalcium phosphate in its dihydrated or anhydrous forms or as mixtures thereof in any desired ratio, tricalcium phosphate and calcium pyrophosphate. Most typically dicalcium phosphate is employed, generally as the dihydrate. Dicalcium phosphate is typically the sole polishing agent, but if desired minor amounts (e.g. up to about 5% by weight of the dental cream and up to about 12% by weight of the total polishing material) of other dentally acceptable water-insoluble polishing agents which do not substantially interfere with the ability of the composition of the invention to promote oral hygiene may be present. Typical polishing agents are alumina, silica, sodium aluminosilicate etc. A minor amount of hydrated alumina (e.g. about 1%) also inhibits or even eliminates the tendency of some dental creams to separate or "bleed" in their tubes.

In the dental cream formulations the dental vehicle comprises a liquid phase proportioned with the gelling agents to form an extrudible creamy mass of desirable consistency. In general, liquids in the dental cream will comprise chiefly water, glycerine, sorbitol, polyethylene glycol 400, propylene glycol, or the like including suitable mixtures thereof. It is advantageous usually to use a mixture of both water and a humectant or binder such as glycerine or sorbitol; typically about 10-30% by weight of water and about 15-50% by weight of humectant. It is preferred to use glycerine or sorbitol. The total liquid content will generally be about 20-80% by weight of the formulation.

Any suitable surface active or detersive material may be included in the dental cream compositions. Such compatible materials are desirable to provide additional detersive, foaming and antibacterial properties depending upon the specific type of surface active material and are selected accordingly. These detergents are water-soluble compounds usually, and may be anionic, nonionic or cationic in structure. It is usually preferred to use the water-soluble non-soap or synthetic organic detergents. Suitable detersive materials are known and include, for example, the water-soluble salts of higher fatty acid monoglyceride monosulphate detergents (e.g. sodium coconut fatty acid monoglyceride monosulphate), higher alkyl sulphates (e.g. sodium lauryl

sulphate), alkyl aryl sulphonates (e.g. sodium dodecyl benzene sulphonate, or higher fatty acid esters of 1,2-dihydroxy propane sulphonate) and the like.

Further surface active agents include the substantially saturated higher aliphatic acyl amides of lower aliphatic amino carboxylic acid compounds, such as those having 12 to 16 carbon atoms in the acyl radical. The amino acid portion is derived generally from the lower aliphatic saturated monoaminocarboxylic acids having about 2 to 6 carbon atoms usually the monocarboxylic acid compounds. Suitable compounds are the fatty acid amides of glycine, sarcosine, alanine, 3-aminopropanoic acid and valine having about 12 to 16 carbon atoms in the acyl group. It is preferred to use the N-lauroyl, myristoyl and palmitoyl sarcoside compounds, however, for optimum effects.

The amide compound may be employed in the form of the free acid or preferably as the water-soluble salts thereof, such as the alkali metal, ammonium, amine and alkylolamine salts. Specific examples thereof are the sodium and potassium N-lauroyl, myristoyl and palmitoyl sarcosides, ammonium and ethanolamine N-lauroyl glycide and alanine. For convenience herein, reference to "amino carboxylic acid compound," "sarcoside," and the like refers to such compounds having a free carboxylic group or the water-soluble carboxylate salts.

Such materials are utilized in pure or substantially pure form. They should be as free as practicable from soap or similar higher fatty acid material which tends to reduce the activity of these compounds. In usual practice, the amount of such higher fatty acid material is less than 15% by weight of the amide and insufficient to substantially adversely affect it, and preferably less than about 10% of the said amide material.

Various other materials may be incorporated in the dental creams of this invention. Examples thereof are colouring or whitening agents, preservatives, stabilisers, tetrasodium pyrophosphate, silicones, chlorophyll compounds and ammoniated materials such as urea, diammonium phosphate and mixtures thereof. These adjuvants are incorporated in the compositions of the present invention in amounts which do not substantially adversely affect the desired properties and characteristics and are suitably selected and used in conventional amounts.

For some purposes it may be desirable to include antibacterial agents in the compositions of the present invention. Typical antibacterial agents which may be used in amounts of about 0.01% to about 5%, preferably about 0.05% to about 1.0%, by weight of the dentifrice composition include:

N^1-4 (chlorobenzyl) - N^5-(2,4-dichlorobenzyl) biguanide;

p-chlorophenyl biguanide;

4-chlorobenzyhydryl biguanide;

4-chlorobenzyhydrylguanylurea;

N-3-lauroxypropyl-N^5-p-chlorobenzylbiguanide;

1,6-di-p-chlorophenylbiguanidehexane;

1-(lauryldimethylammonium)-8-(p-chlorobenzyl-dimethylammonium) octane dichloride;

5,6-dichloro-2-guanidinobenzimidazole;

N^1-p-chlorophenyl-N^5-laurylbiguanide;

5-amino-1,3-bis (2-ethylhexyl)-5-methylhexahydropyrimidine;

and their non-toxic acid addition salts.

Any suitable flavouring or sweetening materials may be employed in formulating a flavour for the compositions of the present invention. Examples of suitable flavouring constituents include the flavouring oils, e.g., oils of spearmint, peppermint, wintergreen, sassaras, clove, sage, eucalyptus, marjoram, cinnamon, lemon and orange, as well as methylsalicylate. Suitable sweetening agents include sucrose, lactose, maltose, sorbitol, sodium cyclamate, the sodium saccharine dipeptides of U.S. Patent No. 3,939,261 and the oxathiazin salts of U.S. Patent No. 3,932,606. Suitably, the flavour and sweetening agents may together comprise from about 0.01 to 5% or more of the compositions.

The dental cream should have a pH practicable for use. A pH range of 5 to 9 is particularly desirable. When the main polishing agent is hydrated alumina, the pH may be 3 to 10.5. The reference to the pH is meant to be the pH determination directly on the toothpastes. If desired, materials such as benzoic acid or citric acid may be added to adjust the pH to, say, 5.5 to 6.5, generally or say 4 to 7.5 for hydrated alumina dental cream.

The dental cream is typically packaged in an extrudible tube, such as lined or unlined aluminium or lead, or laminated tubes generally, and particularly for hydrated alumina dental cream, in mechanical dispensers.

The invention may be put into practice in various ways and a number of specific embodiments will be described to illustrate the invention with reference to the accompanying examples.

The compositions are prepared in the usual manner and all amounts of the various ingredients are by weight unless otherwise specified.

EXAMPLE 1

HIGH VISCOSITY HYDROXYETHYL CELLULOSE-HYDRATED ALUMINA-NON-FLUORIDES AND BINARY FLUORIDE SOURCES

The following dental creams having the formulations given in Table 1 below were prepared by conventional dental cream formulation techniques. Dental creams A and B were filled into the

mechanical dispenser described in published British Patent Application 2,070,695A. Dental cream C was filled into an unlined aluminium dental cream tube and dental cream D was filled into a lined aluminium dental cream tube.

TABLE 1

EXAMPLE	PARTS 1A	1B	1C	1D
Sorbitol (70% solution)	23,000	23,000	------	23,000
Sorbitol	16.1	16.1	------	16.1
Glycerine	------	------	20.20	------
Hydroxyethyl cellulose (Hercules Natrosol 250M)	------	1.00	------	------
Hydroxyethyl cellulose (Hoechst Tylose H 10000P)	1.00	------	1.30	1.00
Alpha alumina trihydrate (Alcoa (Registered Trade Mark) C333)	52,000	52,000	52,000	52,000
C12-C18 Alcohol Na sulphate (100% AI)	0.5	0.5	1.5	1.5
Zinc sulphate .$7H_2O$	------	------	0.48	------
Aluminium sulphate .$18H_2O$	------	------	------	0.78
Sodium saccharin	0.17	0.17	0.20	0.17

TABLE 1 (continued)

EXAMPLE	PARTS 1A	1B	1C	1D
Methyl p-hydroxy-benzoate	0.08	0.08	0.08	------
Sodium monofluoro-phosphate	0.76	0.76	------	------
Sodium fluoride	0.10	0.10	------	------
Pyridyl carbinol	0.10	0.10	------	------
Allantoin	0.15	0.15	0.15	------
Flavour	1.20	1.20	1.00	1.20
Phosphoric acid (85%)	0.14	0.14	------	------
Deionized water	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100

During filling and upon extrusion the surfaces of the dental creams A, C and D were smooth and rheologically desirable while dental cream B underwent extensional rheology during filling and upon extrusion from its container. Similar rheological effects to those exhibited by dental creams A, C and D occurred when Tylose H 10000P of dental creams A, C and D was replaced by Natrosol 250 H and Natrosol 250 HH. Tailing occurred when dental cream B (with Natrosol 250 M) was filled into a dental cream tube.

EXAMPLES 2A to 2E

HIGH VISCOSITY HYDROXYETHYL CELLULOSE-CALCIUM PHOSPHATE-BINARY FLUORIDE SOURCES

The following dental cream having the formulation shown in Table 2 was prepared by conventional

dental cream formulation techniques, placed in an aluminium dental cream tube and extruded by extruding dental cream ribbon twice a day, five days a week for two weeks:

TABLE 2

	PARTS
Glycerine	22.00
Hydroxyethyl cellulose-viscosity 20000-30000 (Hoechst Tylose H10000P)	1.00
Dicalcium phosphate dihydrate	48.00
Sodium lauryl sulphate	1.50
Sodium saccharine	0.20
Sodium monofluorophosphate	0.76
Sodium fluoride	0.10
Flavour	0.90
Deionized Water	Q.S. to 100

The dental cream did not form a tail upon extrusion and was rheologically desirable.

The rheology was also desirable when Tylose H 10000P was replaced by Natrosol 250H (Example 2B) and also when it was replaced by Natrosol 250HH (Example 2C).

When lower viscosity grades of hydroxyethyl cellulose such as Natrosol 250M (Hercules) (Example 2D) or Tylose H 40000P (Example 2E) replace Tylose H 10000 P, a tail formed upon extrusion of the dental cream. Examples 2D and 2E are comparison examples.

* C L M S *

CLAIMS

1. A dental cream comprising about 20-75% by weight of a polishing material, at least about half of which is hydrated alumina and about 20-80% by weight based on the weight of the dental cream of a liquid phase containing water, humectant or a mixture thereof and about 0.5-5% by weight based on the weight of the dental cream of a gelling agent consisting essentially of hydroxyethyl cellulose having a viscosity in a range the average of which is at least about 24000 cps, determined on a Brookfield viscometer in 2% by weight water: glycerine (1:1.56) solution at 20°C, with a No. 6 spindle at 20 rpm.

2. A dental cream as claimed in Claim 1 in which the hydrated alumina is present in an amount of about 40-55% as alpha-alumina trihydrate.

3. A dental cream as claimed in Claim 1 or Claim 2 in which the said dental cream is contained in a pressure differential dispensing container, a mechanically operated dispensing container or a dental cream tube.

4. A dental cream as claimed in Claim 3 in which the said dental cream is contained in a mechanically operated dispensing container from which it is extrudible.

5. A dental cream as claimed in Claim 3 in which the said dental cream is contained in a dental cream tube.

6. A dental cream as claimed in Claim 5 in which the said dental cream tube is an unlined aluminium tube.

7. A dental cream as claimed in any one of Claims 1 to 6 in which fluoride-providing compound is present in an amount which provides about 100-10000 ppm of fluorine.

8. A dental cream as claimed in Claim 7 in which the said fluoride is provided by sodium monofluorophosphate in an amount of about 750-2000 ppm.

9. A dental cream as claimed in Claim 7 in which about 750-2000 ppm of fluoride is provided by a binary fluoride system of sodium monofluorophosphate and sodium fluoride in which about 30-40% by weight of the fluoride is provided by sodium fluoride.

10. A dental cream as claimed in any one of Claims 1 to 7 or 1 to 7 and 8 in which zinc sulphate or aluminium sulphate is present in an amount of about 0.05-1.5% by weight.

11. A dental cream comprising a binary fluoride source of a mixture of sodium monofluorophosphate and sodium fluoride in which about 30-40% by weight of the said fluoride is from the said sodium fluoride, in an amount to provide 750-2000 ppm total of ionic fluorine, about 35-75% by weight of a polishing agent consisting essentially of calcium phosphate and a dental vehicle comprising about 20-80% by weight based on the weight of the dental cream of a liquid phase containing water, humectant or a mixture thereof and about 0.5-5% by weight based on the weight of the dental cream of a gelling agent consisting essentially of hydroxyethyl cellulose having a viscosity in a range the average of which is at least about 24000 cps, determined on a Brookfield viscometer in 2% water:glycerine (1:1.56) aqueous solution at 20°C, with a No. 6 spindle at 20 rpm.

12. A dental cream as claimed in Claim 11 in which the said binary fluoride source provides about 1400 2000 ppm of ionic fluroine.

13. A dental cream as claimed in Claim 10 or Claim 11 in which dicalcium phosphate is present as polishing agent in amount of about 40-75% by weight.

14. A dental cream as claimed in any one of Claims 1 to 13 in which the said hydroxyethyl cellulose is a grade having a viscosity of about 17000-31000; about 37000-41000 or about 20000-30000.

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15. A dental cream as claimed in Claim 14 in which the said hydroxyethyl cellulose has a viscosity of about 20000-30000.

16. A dental cream as claimed in any one of Claims 1 to 15 in which the said gelling agent is present in an amount of about 0.8-2% by weight.

17. A dental cream as claimed in Claim 1 and Example 1 or Example 2.