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(57) Abstract

The subject invention encompasses adhesive compositions comprising unmixed partial salts of a lower alkyl vinyl ether-maleic acid copolymer and polyethylene glycol having an average molecular weight of above about 100 and equal to or below about 600.

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DENTURE STABILIZING COMPOSITIONS

BACKGROUND

Ordinary removable dentures, dental plates and the like, comprise teeth mounted in a suitable plate or base. Although dentures generally are skillfully prepared, often they do not fit perfectly. Moreover, no matter how satisfactory at first, after a period of time the fit of the denture becomes loose and imperfect due to natural shrinkage and changes in the gums, mucous tissues, and the like. Loose and imperfectly fitted dentures usually are corrected and stabilized by the use of a denture stabilizer. Denture stabilizers are used to fill the interstices between the dentures and the gums or tissues. Prior to placement of the denture in the oral cavity, a denture stabilizer is applied to the denture-plate surface which, for a perfect fit, should uniformly contact the gums and mucous tissues. The denture stabilizer is formulated not only for its adherent properties, but also to provide a cushion or gasket between the denture and the gums or tissues, thereby positioning the denture securely in the oral cavity.

Several deficiencies that commonly exist with denture stabilizing or adhesive compositions are phase separation, the need for more than one application of the adhesive per day and oozing of the adhesive from under the dental plate. Oozing is particularly undesirable because of the resulting unpleasant taste, unpleasant mouthfeel, and loss of adhesive from under the dental plate.

Considerable effort has been made over the years to develop improved denture adhesive compositions. Both synthetic and natural polymers and gums have been used singly, in combination, and in combination with various adhesives in an attempt to lessen the deficiencies noted above. However, the need still exists for improved denture stabilizing compositions which offer a secure hold, are aesthetically pleasing to the user, which ooze less than currently available products, and which are easy to clean from the mouth and/or denture.

It has been discovered, in accordance with the present invention, that a denture stabilizer can be formulated having excellent adhesive quality while oozing less and providing pleasing aesthetics to the user. The invention adhesive compositions may also be effectively used as a wound dressing, underwater adhesive, bio-adhesive, and/or as a delivery vehicle for other actives.

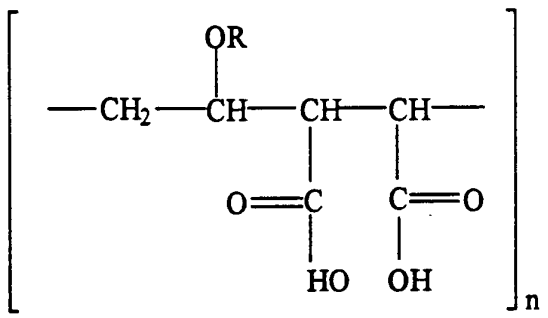
It is an object of the present invention to provide a denture stabilizing composition which effectively holds dentures in place for prolonged periods of time yet allows for easy removal of the denture on demand. It is also an object of the invention to provide an improved denture stabilizing composition which oozes less than currently available stabilizers and is aesthetically pleasing to the user. It is a further object that the hydrophilic nature of the invention compositions will provide adhesive compositions that are easier to clean from the mouth and/or denture than currently available products.

These and other objects of the present invention will become readily apparent from the detailed description which follows.

SUMMARY OF THE INVENTION

The present invention encompasses adhesive compositions comprising: a) from about 10% to about 80% of an unmixed partial salt of a lower alkyl vinyl ether-maleic acid copolymer consisting essentially of the repeated structural unit:

(I)



wherein R represents a C1 to C4 alkyl radical, n is an integer greater than one representing the number of repeated occurrences of the structural unit in a molecule of the copolymer and n is large enough to characterize the copolymer as having a specific viscosity larger than 1.2, the specific viscosity being determined in methyl ethyl ketone at 25C, and wherein the partial salt contains a cationic salt function of from about 0.1% to about 60% zinc or strontium cations, of the total initial carboxyl groups reacted; and b) from about 20% to about 90% of polyethylene glycol having an average molecular weight above about 100 and equal to or below about 600.

DETAILED DESCRIPTION OF THE INVENTION

The adhesive compositions of the present invention comprise lower alkyl vinyl ether-maleic acid copolymers consisting of unmixed zinc or strontium salts, and polyethylene glycol . Polyethylene glycol having an average molecular weight of about 400 is most preferred for use in the present invention compositions. The present compositions may be formulated as creams, pastes, powders, liquids,

ointments, and lotions. A detailed description of essential and optional components of the present invention is given below.

Lower Alkyl Vinyl Ether-Maleic Acid Copolymer Salts

The present adhesive compositions comprise an unmixed partial salt of a lower alkyl vinyl ether-maleic acid ("AVE/MA") copolymer consisting essentially of the repeated structural unit:

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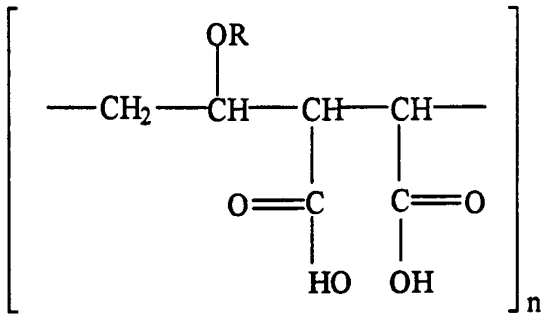


wherein R represents a C1 to C4 alkyl radical, n is an integer greater than one representing the number of repeated occurrences of the structural unit in a molecule of the copolymer and n is large enough to characterize the copolymer as having a specific viscosity larger than 1.2, the specific viscosity being determined in methyl ethyl ketone at 25C, and wherein the partial salts contain a cationic salt function of from about 0.1% to about 60% zinc (preferred) or strontium cations, preferably from about 10% to about 60%, and most preferably from about 20% to about 50%, of the total initial carboxyl groups reacted.

The term "unmixed copolymer salts" as used herein refers to zinc and strontium partial salts of lower alkyl vinyl ether-maleic acid copolymers wherein the zinc or strontium cations are unmixed with any other ester functions or nonidentical cations on the same copolymer, the remaining carboxyl groups being unreacted.

The term "mixed copolymer salts" as used herein refers to zinc and/or strontium partial salts of lower alkyl vinyl ether-maleic acid copolymers wherein the zinc and strontium are mixed on the same copolymer with each other, or with other ester functions or nonidentical cations selected from the group consisting of calcium, sodium, magnesium, potassium, ammonium, and mixtures thereof.

It is preferred that the present compositions further comprise from about 0.1% to about 75% of one or more mixed partial salts of lower alkyl vinyl ether-maleic acid copolymers wherein the partial salts contain a cationic salt function selected from the group consisting of calcium, sodium, magnesium, potassium,

ammonium, zinc, strontium, and mixtures thereof. Most preferred are mixed copolymer salts containing zinc, calcium, or sodium cations, or mixtures thereof. Zinc cations may be present at a level of from about 0.1% to about 65%, preferably from about 10% to about 45%, and most preferably from about 15% to about 30%, of the total initial carboxyl groups reacted. Calcium ions may be present at a level of from about 10% to about 75%, preferably from about 25% to about 60%, and most preferably from about 40% to about 60%, of the total initial carboxyl groups reacted. Sodium cations may be present at a level of from about 1% to about 20%, preferably from about 1% to about 15%, and most preferably from about 1% to about 10%, of the total initial carboxyl groups reacted.

The subject polymeric salts are advantageously prepared by the interaction of the AVE/MA copolymer (I) with cationic zinc or strontium compounds having a functional group typical of reactants of a carboxylic acid, such as, for example, the hydroxide, acetate, halide, lactate, etc. in an aqueous medium. In a preferred embodiment, mixed AVE/MA copolymer salts are prepared by the interaction of the AVE/MA copolymer (I) with cationic calcium, sodium, magnesium, potassium, ammonium, zinc, strontium (and mixtures thereof) compounds having a functional group as specified above for cationic zinc or strontium compounds. In a preferred mixed AVE/MA copolymer embodiment, the oxide of zinc and the hydroxide of calcium are utilized.

Since zinc hydroxide is not commercially available, its use as a reactant is readily and more economically accomplished by employing an aqueous slurry of particular zinc oxide which, although practically insoluble in water, provides hydration to zinc hydroxide on the particulate surface. Strontium hydroxide, on the other hand, is available in either crystalline or powder form and is soluble in about 50 parts water. Aqueous solutions of strontium oxide, however, which forms the hydroxide when treated with water (caution: heat evolution), may also be used.

Anions that form toxic, irritating or contaminating by-products should be avoided, or special precautions and treatment provided to assure the removal and absence of such by-products from the polymeric salt end-product. The particular compound used should be substantially pure to assure obtaining a substantially pure, substantially off-white polymeric salt end-product.

The lower alkyl vinyl ether maleic acid (AVE/MA) copolymers are readily obtained by copolymerizing a lower alkyl vinyl ether monomer, such as methyl vinyl ether, ethyl vinyl ether, divinyl ether, propyl vinyl ether and isobutyl vinyl ether, with maleic anhydride to yield the corresponding lower alkyl vinyl ether-maleic anhydride copolymer which is readily hydrolyzable to the acid copolymer (I). Both anhydride

and acid forms are also available from commercial suppliers. For example, the GAF Corporation, Wayne, N.J. provides both the polymeric free acid form (I) and the corresponding anhydride form under its "GANTREZ" trademark as the "GANTREZ S Series" and "GANTREZ AN Series", respectively. In the former acid series, the GANTREZ S-97 (M. W. TM 50,000) is particularly suitable, and, in the latter anhydride series, the GANTREZ AN-149 (M. W. = 50,000) the GANTREZ AN-169 (M. W. = 67,000) and the GANTREZ AN-179 (M. W. = 80,000) copolymers are particularly suitable. The acid and anhydride forms of AVE/MA copolymers, having an average molecular weight of from about 50,000 to about 80,000 (as measured by membrane osmometry in 2-butanone 1-10 grams/1000 ml solution), are also characterized by having the previously described specific viscosity parameter of more than 1.2. When the anhydride copolymer dissolves in water, the anhydride linkage is cleaved so that the highly polar, polymeric free acid (I) is formed. Accordingly, the anhydride form, which is relatively less expensive than the acid form, may be used as a convenient and cheaper precursor for the acid. Elevated temperatures may be advantageously employed to enhance the rate of anhydride-to-acid hydrolysis.

In general, the lower alkyl vinyl ether-maleic acid copolymer (I), or its corresponding anhydride, is added to water preheated to about 70°-80°C. with vigorous stirring to form a homogeneous mixture. If the anhydride precursor is utilized, it is recommended that the aqueous mixture be further heated to about 90° C. with stirring to ensure complete hydrolysis of the anhydride to the acid form. Heating is then discontinued although mixing is continued until the batch turns clear with a simultaneous decrease in viscosity (about 65°-75°C.). An aqueous solution of the cationic zinc or strontium salt forming compound, or, for example, an aqueous dispersion of particulate zinc oxide in the form of a slurry, in an amount sufficient to provide the desire cationic content desired in the end-product, is separately prepared at ambient temperature and slowly added to the hot polymeric acid solution with continuous vigorous mixing so as to prevent localized precipitation of the cationic polymeric salt. After addition is complete, mixing is continued to ensure that all the salt forming compound is reacted with the copolymer.

Alternatively, an aqueous solution containing the zinc or strontium source is preheated to 70°-80°C. with vigorous stirring to form a homogeneous slurry. The lower alkyl vinyl ether-maleic acid copolymer (I) or its corresponding anhydride is then added to the slurry while further heating to 90°C. and stirring to ensure complete hydrolysis.

The reaction batch is then dried such as by shallow drying trays in a convection oven maintained at about 70°C. with hot air circulation to evaporate the

water content and recover the polymeric salt product in dry form. Alternatively, the reaction batch is then transferred to 5 drum dryers maintained at 80-100 PSIG with hot steam to evaporate the water content and recover the polymeric salt in the flake form.

The resulting flakes may be subjected to milling and screening to yield the desired physical properties to provide satisfactory denture stabilizing properties.

The salts are friable so that appropriate particle size and bulk density can be obtained. For best results, particles should be capable of passage through a 140- to 200-mesh sieve (U.S.B.S. series) and preferably are less than 0.74 millimeter in their largest dimension.

The subject zinc or strontium AVE/MA copolymer salts have exceptional adhesive qualities when contacted with water or saliva such that they are extremely useful as denture adhesive materials in denture stabilizing compositions. For such use the salt in particulate form is preferably characterized by a particle size of at least minus 140-mesh U.S.B.S. sieve; a bulk density greater than 0.3 gram per cubic centimeter and preferably higher than 0.6 gram per cubic centimeter; and a pH between 3 and 7.0, the pH being determined on a one percent by weight dispersion in water.

The subject zinc or strontium AVE/MA copolymer salts may be utilized in effective adhesive amounts, preferably at least 20 percent by weight, as the sole adhesive component or as a co-adhesive in joint usage with other active adhesive components in denture stabilizing compositions. Preferably, the unmixed zinc or strontium AVE/MA copolymer salts may be utilized with mixed AVE/MA copolymer salts containing cations such as calcium, sodium, magnesium, potassium, ammonium, zinc, strontium, and mixtures thereof.

Polyethylene Glycol

The invention compositions also comprise polyethylene glycol. In general, polyethylene glycols are polymers with the general formula (OCH2CH2)nOH, where n is greater than or equal to 4. The polyethylene glycols are designated by a number that represents the average molecular weight [Merck Index, Tenth Edition, No. 7441, 1983].

The present compositions comprise polyethylene glycol having an average molecular weight above about 100 and equal to or below about 600. Preferred is polyethylene glycol having an average molecular weight of equal to or greater than about 300 and equal to or below about 600. Polyethylene glycol having an average molecular weight of about 400 is most preferred. The polyethylene glycols suitable

for use in the present invention are well known and commercially available, such as those marketed by Union Carbide Corporation under the trademark "Carbowax".

The level of polyethylene glycol that is useful in the present invention is based on compositions containing AVE/MA copolymer salts characterized by a particle size of at least minus 140-mesh U.S.B.S. sieve. Therefore, polyethylene glycol having an average molecular weight above about 100 and equal to or below about 600 is present at a level of from about 20% to about 90%, preferably from about 30% to about 80%, and most preferably from about 35% to about 75%, by weight of the invention compositions.

Optional components

The present invention compositions may also include a safe and adhesively effective amount of a co-adhesive. The term "safe and adhesively effective amount" as used herein means an amount sufficient to provide adherence of a denture or dental prosthesis to the oral cavity.

Preferred co-adhesives include a water-soluble hydrophilic colloid or polymer having the property of swelling upon exposure to moisture to form a mucilaginous mass. Such adhesive materials include natural gums, synthetic polymeric gums, adhesive materials commonly employed in denture stabilizing compositions and compatible with the subject AVE/MA copolymer salts, synthetic polymers, saccharide derivatives, cellulose derivatives, and mixtures thereof. Examples of such materials include karaya gum, guar gum, gelatin, algin, sodium alginate, tragacanth, methylcellulose, acrylamide polymers, ethylene oxide polymers, polyvinylpyrrolidone, cationic polyarylamide polymers, carboxymethylcellulose, sodium carboxymethylcellulose and mixed partial salts of poly(vinyl methyl-ether maleate). Sodium carboxymethylcellulose is most preferred for use in the present invention. In general, the co-adhesives may be present at a level of from about 5% to about 70% by weight of the composition.

Other suitable optional ingredients include colorants; preservatives such as methyl and propyl parabens; thickeners such as silicon dioxide, and polyethylene glycol having an average molecular weight of 8000; and vehicles such as liquid petrolatum, petrolatum, mineral oil, and glycerin. Preferred are polyethylene glycol having an average molecular weight of 8000, mineral oil, and petrolatum. Colorants, preservatives, thickeners, and vehicles may be present at levels of from about 0% to about 20%, by weight of the composition.

The compositions of the present invention may optionally include from about 0.01% to about 5% of one or more components which provide the user with sensory, including flavor, benefits. Suitable components include natural or artificial

sweetening agents, menthol, methyl lactate, wintergreen oil, peppermint oil, spearmint oil, leaf alcohol, as well as coolants 3-l-menthoxypropane-1,2-diol and paramenthane carboxyamide agents such as N-ethyl-p-menthane-3-carboxamide which is described in U.S. Patent 4,136,163 to Watson et. al., which is incorporated by reference herein in its entirety.

The compositions of the present invention are manufactured in an art-recognized manner known to those skilled in the art, such as powder, cream, ointment, liquid, or paste formulations. Suitable examples of such formulations are disclosed in U.S. Patent 4,518,721, issued May 21, 1985, and U.S. Patent 4,514,528, issued April 30, 1985, both to Dhabar et al., and both incorporated by reference herein in their entirety.

The following non-limiting examples illustrate embodiments of the subject invention wherein both essential and optional ingredients are combined. These examples are given solely for the purpose of illustration and are not to be construed as limiting the scope of the invention

EXAMPLE I

Ingredients	Weight %
17.5% Zinc unmixed partial salt of AVE/MA copolymer(a)	33.0
Polyethylene Glycol 400	40.5
Sodium Carboxymethylcellulose	17.3
Petrolatum	8.0
Polyethylene Glycol 8000	1.2

(a) AVE/MA copolymer salt having about 17.5% neutralization with zinc.

EXAMPLE II

Ingredients	Weight %
20.0% Strontium unmixed partial salt of AVE/MA copolymer(a)	10.0
47.5% Calcium/17.5% Zinc mixed partial salt of AVE/MA copolymer(b)	28.1
Polyethylene Glycol 400	39.0
Sodium Carboxymethylcellulose	12.1
Petrolatum	10.0
Mineral Oil	0.8

(a) AVE/MA copolymer salt having about 20% neutralization with strontium.

(b) AVE/MA copolymer salt having about 47.5% neutralization with calcium and about 17.5% neutralization with zinc.

EXAMPLE III

	Weight %
25% Zinc unmixed partial salt of AVE/MA copolymer[a]	11.9
65% Calcium partial salt of AVE/MA copolymer [b]	24.1
Polyethylene Glycol 400	42.2
Sodium Carboxymethylcellulose	12.8
Petrolatum	8.0
Polyethylene Glycol 8000	1.0

(a) AVE/MA copolymer salt having about 25% neutralization with zinc.

(b) AVE/MA copolymer salt having about 65% neutralization with calcium.

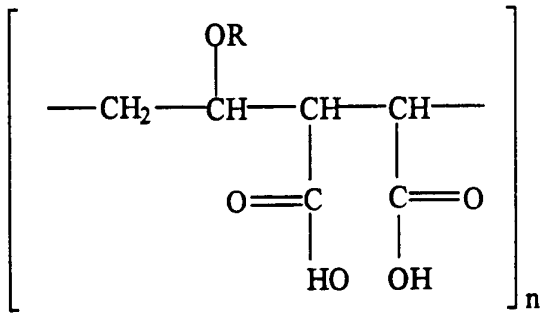
Examples I-III are prepared as follows. Combine polyethylene glycol 400, petrolatum, (and mineral oil if present) and heat to 55-65°C until liquid. Add sodium carboxymethylcellulose, polyethylene glycol 8000, and AVE/MA copolymer salts. Stir until well mixed. Cool to room temperature.

What is claimed is:

1 An adhesive composition comprising:

a) from 10% to 80% of an unmixed partial salt of a lower alkyl vinyl ether-maleic acid copolymer consisting essentially of the repeated structural unit:

(I)



wherein R represents a C1 to C4 alkyl radical, n is an integer greater than one representing the number of repeated occurrences of the structural unit in a molecule of the copolymer and n is large enough to characterize the copolymer as having a specific viscosity larger than 1.2, the specific viscosity being determined in methyl ethyl ketone at 25C, and wherein the partial salts contain a cationic salt function of from 0.1% to 60% zinc or strontium cations, of the initial carboxyl groups reacted; and

b) from 20% to 90% of polyethylene glycol having an average molecular weight above 100 and equal to or below 600.

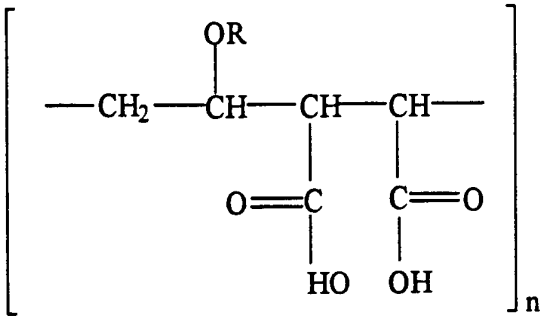
2. The composition according to Claim 1 further comprising from 0.1% to 75% of one or more mixed partial salts of lower alkyl vinyl ether-maleic acid copolymers wherein the partial salts contain a cationic salt function selected from the group consisting of calcium, sodium, magnesium, potassium, ammonium, zinc, strontium, and mixtures thereof.

3. The composition according to Claim 2 comprising from 20% to 90% of polyethylene glycol having an average molecular weight of equal to or greater than 300 and equal to or below 600.

4. An adhesive composition comprising:

a) from 20% to 70% of an unmixed partial salt of a lower alkyl vinyl ether-maleic acid copolymer consisting essentially of the repeated structural unit:

(I)



wherein R represents a C1 to C4 alkyl radical, n is an integer greater than one representing the number of repeated occurrences of the structural unit in a molecule of the copolymer and n is large enough to characterize the copolymer as having a specific viscosity larger than 1.2, the specific viscosity being determined in methyl ethyl ketone at 25C, and wherein the partial salts contain a cationic salt function of from 0.1% to 60% zinc or strontium cations, of the total initial carboxyl groups reacted; and

b) from 30% to 80% of polyethylene glycol having an average molecular weight above 100 and equal to or below 600.

5. The composition according to Claim 4 further comprising from 0.1% to 75% of one or more mixed partial salts of lower alkyl vinyl ether-maleic acid copolymers wherein the partial salts contain a cationic salt function selected from the group consisting of calcium, sodium, magnesium, potassium, ammonium, zinc, strontium, and mixtures thereof.

6. The composition according to Claim 5 comprising from 30% to 80% of polyethylene glycol having an average molecular weight of equal to or greater than 300 and equal to or below 600.

7. The composition according to Claim 6 wherein (a) is zinc.

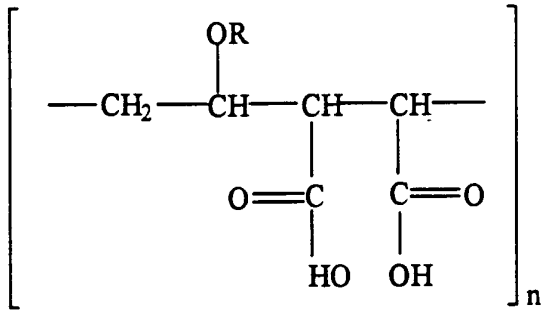
8. The composition according to Claim 7 further comprising optional components selected from the group consisting of colorants, preservatives, thickeners, vehicles, and mixtures thereof.

9. The composition according to Claim 8 further comprising a safe and adhesively effective amount of a co-adhesive selected from the group consisting of natural gums, synthetic polymeric gums, synthetic polymers, saccharide derivatives, cellulose derivatives, and mixtures thereof.

10. An adhesive composition comprising:

a) from 25% to 65% of an unmixed partial salt of a lower alkyl vinyl ether-maleic acid copolymer consisting essentially of the repeated structural unit:

(I)



wherein R represents a C1 to C4 alkyl radical, n is an integer greater than one representing the number of repeated occurrences of the structural unit in a molecule of the copolymer and n is large enough to characterize the copolymer as having a specific viscosity larger than 1.2, the specific viscosity being determined in methyl ethyl ketone at 25C, and wherein the partial salts contain a cationic salt function of from 10% to 60% zinc or strontium cations, of the total initial carboxyl groups reacted;

b) a mixed partial salt of a lower alkyl vinyl ether-maleic acid copolymer wherein the partial salt contains a cationic salt function of from 0.1% to 65% zinc or strontium cations, and from 10% to 75% calcium cations, of the total initial carboxyl groups reacted; and

c) from 35% to 75% of polyethylene glycol having an average molecular weight of 400.

11. The composition according to Claim 10 wherein (a) is zinc.

12. The composition according to Claim 11 further comprising optional components selected from the group consisting of colorants, preservatives, thickeners, vehicles, and mixtures thereof.

13. The composition according to Claim 12 further comprising a safe and adhesively effective amount of a co-adhesive selected from the group consisting of natural gums, synthetic polymeric gums, synthetic polymers, saccharide derivatives, cellulose derivatives, and mixtures thereof.

14. The composition according to Claim 13 wherein the mixed partial salt further comprises a cationic salt function of from 1% to 20% sodium cations.

INTERNATIONAL SEARCH REPORT

Inter ial Application No
PCT/US 95/07280

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K6/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP,A,0 121 692 (RICHARDSON VICKS INC) 17 October 1984 see page 7, line 32 - page 9, line 36 see page 13, line 6 - page 14, line 5 see claims & US,A,4 514 528 cited in the application	1-14
A	EP,A,0 265 916 (RICHARDSON VICKS INC) 4 May 1988 see page 2, line 19 - line 47; claims	1-14

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
6 October 1995	16.10.95

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax (+31-70) 340-3016	Cousins-Van Steen, G

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Interr al Application No
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		AU-B-	590988	23-11-89
		AU-B-	8016287	28-04-88
		CA-A-	1274044	11-09-90
		DE-A-	3786981	16-09-93
		DE-T-	3786981	24-02-94
		IE-B-	60905	24-08-94
		JP-A-	63128009	31-05-88
		ZA-A-	8707882	22-04-88