

(43) International Publication Date
25 September 2014 (25.09.2014)

(51) International Patent Classification:

A61Q 11/00 (2006.01) C08F 222/02 (2006.01)
C08F 220/06 (2006.01)

(21) International Application Number:

PCT/US2014/025730

(22) International Filing Date:

13 March 2014 (13.03.2014)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

61/792,711 15 March 2013 (15.03.2013) 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: ITACONIC ACID POLYMERS FOR ORAL CARE APPLICATIONS

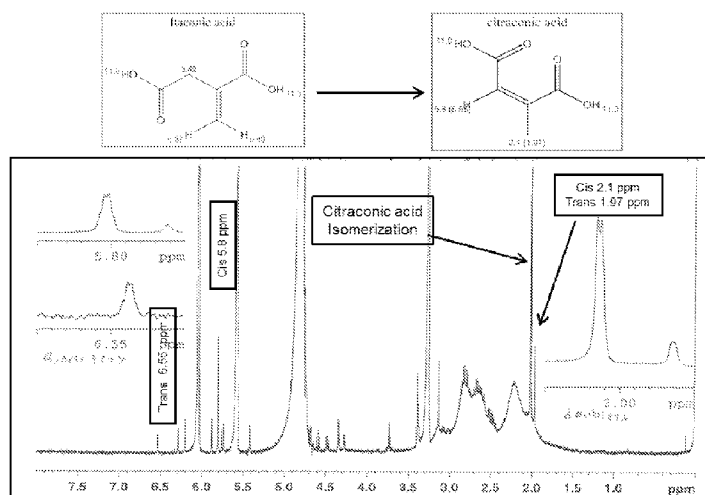


FIG. 1

(57) Abstract: The disclosed technology relates to an oral care composition comprising a pure polyitaconic acid homo- or co-polymer free of the less reactive tri-substituted vinyl monomers (e.g., citraconic acid or mesaconic acid).



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- *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

TITLE

ITACONIC ACID POLYMERS FOR ORAL CARE APPLICATIONS

BACKGROUND OF THE INVENTION

[0001] The disclosed technology relates to an oral care composition comprising a pure polyitaconic acid homo- or co-polymer free of the less reactive tri-substituted vinyl monomers (e.g., citraconic acid or mesaconic acid).

[0002] There are several process patents in the prior art that provide processes to produce itaconic acid (IA) homopolymer. A common thread in the prior art is the use of neutralization in the process. For example, U.S. Pat. No. 5,223,592 reports that the critical aspect in preparing itaconic acid is to provide complete neutralization of an itaconic acid type monomer prior to conducting the polymerization reaction. Complete neutralization is identified as having two moles of base neutralizer for each mole of itaconic acid. Similarly, U.S. Pat. No. 5,336,744 discloses a process using from 5 to 50% neutralization along with a polyvalent metal ion and an initiator. Another US patent, U.S. Pat. No. 7,910,676 from the University of New Hampshire teaches a process using a partial degree of neutralization (25-75%) and an initiator to make a high molecular weight polymer. The itaconic acid polymerization process involving a neutralization step according to the foregoing references leads to a rearrangement of di-substituted itaconic acid derived monomers to the less reactive tri-substituted vinyl monomers (e.g., citraconic acid or mesaconic acid derived monomers). Such isomerization to the tri-substituted monomers results in polymers with unreacted residuals and subsequently causes reduced chelating efficiency.

[0003] In contrast, polymerization of itaconic acid in acidic medium does not favor the rearrangement of itaconic to less reactive citraconic acid. Polymerization of itaconic acid in an acidic medium has been reported in "Polymerization of itaconic acid and some of its derivatives" Marvel et al, Journal of Organic Chemistry, (1959), 24, 599, and in "Polymerization of Itaconic Acid In Aqueous Solution: Structure Of The Polymer And Polymerization Kinetics At 25°C Studied By Carbon-13 NMR," Grespos et al, Makromolekulare Chemie, Rapid Communications (1984), 5(9), 489-494. However, these methods have disadvantages such as poor conversion with lengthy polymerization times and corrosivity issues. Similarly, WO 2001/21677 describes an itaconic acid polymerization comprising a free radical generator (persulfate) and a phosphorous-containing reducing agent.

[0004] US 4,485,223 teaches an "essentially homogenous" (meth)acrylic acid/itaconic acid copolymer. The process taught in the '223 patent teaches a post-neutralization step, and process temperatures ranging from 80 to 120°C, as well as an initiator amount of from 5 to 20 mole%. The level of initiator required in the post-neutralization step of the '223 process results in a corrosive copolymer solution (pH < 1), which has significant safety concerns from a handling point of view that would make scale-up difficult. Moreover, the high initiator level used in the polymerization step taught in the '223 patent gives a dark colored copolymer with a strong unpleasant sulfur odor that would not be suitable for use in the personal care or homecare market. The high temperatures used in the '223 process causes the initiator to decompose quickly, causing oxidized and/or sulfurized itaconic acid impurities resulting in poor performance and potential health concerns with use in the final application.

[0005] Itaconic acid polymers and co-polymers having improved purity, and being free of tri-substituted vinyl monomer isomerization that provide improved stain resistant capabilities in dental care applications, along with methods of preparing the same would be desirable.

SUMMARY OF THE INVENTION

[0006] The disclosed technology, therefore, solves the problem of inefficient stain prevention capability in current dental care applications by providing polymers or co-polymers, that are derived from substantially pure itaconic acid and that are free of tri-substituted vinyl monomers.

[0007] In one aspect, there is provided an oral care composition including a safe and effective amount of a homopolymer or copolymer or salts thereof. The copolymer can contain from about 10 mole percent to about 90 mole percent itaconic acid derived monomer groups. The copolymer can also contain from about 10 mole percent to about 90 mole percent of at least one of: (meth)acrylic acid derived monomer groups, poly unsaturated monomer groups, and combinations thereof. The oral care formulations include dentifrice or gel and mouthwash (e.g., spray, rinse, solutions and suspensions). Other types of oral care formulations include denture adhesives, denture cleaning products, dental composites, tooth whiteners, tooth varnishes, lozenges and chewing gum. The copolymer will be transparent, or substantially transparent.

[0008] In another aspect, the copolymer included in the oral care composition can be prepared at a reaction temperature of between about 60 to about 85°C in the presence of from about 0.01 to about 5 mole percent polymerization initiator, based on the total amount of said monomer groups, and less than 5 equivalent% of a neutralizer per total itaconic acid monomer acid group.

[0009] In an embodiment, the oral care composition can contain from about 0.01% to about 20.0% by weight of the copolymer.

[0010] In a further aspect, there is provided a method of preventing stains on hydroxyapatite, which is considered as a model compound of enamel due to the chemical similarity. The method can include the step of applying to the hydroxyapatite surface a safe and effective amount of a copolymer as described above, or salts thereof.

BRIEF DESCRIPTION OF THE DRAWINGS

[0011] **Figure 1:** ^1H NMR of Comparative Sample I

[0012] **Figure 2:** ^1H NMR of Comparative Sample II

[0013] **Figure 3:** ^1H NMR of Sample 5

DETAILED DESCRIPTION OF THE INVENTION

[0014] Various preferred features and embodiments will be described below by way of non-limiting illustration.

[0015] A first aspect of the invention is an oral care composition including a safe and effective amount of a homopolymer or copolymer or salts thereof.

[0016] The copolymer can be a homogenous or substantially homogenous polymer, or a random or block copolymer or terpolymer or crosslinked polymer ("improved polymers") providing improved stain prevention for oral care applications. The improved polymers can comprise, consist essentially of, or consist of itaconic acid derived monomer groups.

[0017] Itaconic acid is an organic compound which is non-toxic and may be derived from renewable resources. Homopolymers of itaconic acid are biodegradable. Itaconic acid may be obtained by the distillation of citric acid or by the fermentation of carbohydrates such as glucose using *Aspergillus terreus*. Itaconic acid may be referred to as methylenesuccinic acid or 2-methylidenebutanedioic

acid. Itaconic acid may be represented by the formula $C_5H_6O_4$ or by the formula $CH_2=C(COOH)CH_2COOH$.

[0018] The improved polymer may be a homopolymer of itaconic acid wherein the polymer backbone comprises structural units derived from itaconic acid, or an anhydride or salt thereof (collectively referred to as itaconic acid).

[0019] The improved polymer can contain monomer units derived from itaconic acid. Preferably, the improved polymer can contain greater than about 10 mole%, or 50 mole%, preferably greater than 70 mole%, or from about 60 mole% to about 65 or 70 mole% monomer units derived from itaconic acid. In certain instances the monomer units derived from itaconic acid can be from about 1 to about 99 mole%, or about 5 to about 95 mole%, or even about 10 to about 90 mole%, and in some instances from about 20 to about 80 mole%, or about 30 to about 70 mole %, or even from about 40 to about 60 mole %.

[0020] The improved polymer can also comprise, consist of, or consist essentially of (in addition to itaconic acid derived monomer groups) at least one of: C_1 - C_{18} alkyl (meth)acrylates where the alkyl group may be a straight chain group or branched chain group. The alkyl group may be substituted with one or more hydroxyl groups, alkoxy groups, or a mixture thereof. The monomers that may be used may include methyl acrylate, ethyl acrylate, butyl acrylate, 2-hydroxyethyl acrylate, 2-hydroxyethyl methacrylate, phosphate containing monomers, stearyl acrylate, polyethyleneglycol monomethylether acrylate, acrylamide, C_1 - C_{18} N-alkyl (meth)acrylamide, styrene and substituted styrene, vinyl esters such as vinyl acetate, acrylic acid and its sodium salt, 2-acrylamido-2-methylpropane sulfonic acid and its salts (AMPSTM, a registered trademark of the Lubrizol Corporation), acrylamido methanesulfonic acid and its sodium salt, maleic acid and its sodium

salt, (meth)acrylonitrile, or a mixture of two or more thereof. The amount of co-monomer in the copolymer may be up to about 50% by weight of the copolymer or up to 90% by weight, or from about 5 to about 50%, or from 10% to about 40%, or from about 15% to about 20 or 30% by weight of the copolymer. The amount of itaconic acid (the itaconic acid, itaconic anhydride, and the itaconic acid from the salt form of itaconic acid combined) is desirably at least 50, more desirably at least 70, and preferably at least 80% by weight of said polymer or copolymer derived from itaconic acid.

[0021] The improved crosslinked itaconic acid copolymers may comprise ethylenically polyunsaturated compounds containing at least two polymerizable ethylenically unsaturated moieties. Exemplary polyunsaturated crosslinking monomer components include di(meth)acrylate compounds such as ethylene glycol di(meth)acrylate, polyethylene glycol di(meth)acrylate, triethylene glycol di(meth)acrylate, 1,3-butylene glycol di(meth)acrylate, 1,6-butylene glycol di(meth)acrylate, 1,6-hexanediol di(meth)acrylate, neopentyl glycol di(meth)acrylate, 1,9-nonanediol di(meth)acrylate, 2,2'-bis(4-(acryloxy-propyloxyphenyl)propane, and 2,2'-bis(4-(acryloxydiethoxy-phenyl)propane; tri(meth)acrylate compounds such as, trimethylolpropane tri(meth)acrylate, trimethylolethane tri(meth)acrylate, and tetramethylolmethane tri(meth)acrylate; tetra(meth)acrylate compounds such as ditrimethylolpropane tetra(meth)acrylate, tetramethylolmethane tetra(meth)acrylate, and pentaerythritol tetra(meth)acrylate; hexa(meth)acrylate compounds such as dipentaerythritol hexa(meth)acrylate; allyl compounds such as allyl (meth)acrylate, diallylphthalate, diallyl itaconate, diallyl fumarate, and diallyl maleate; polyallyl ethers of sucrose having from 2 to 8 allyl groups per molecule, polyallyl ethers of pentaerythritol such as pentaerythritol diallyl ether, pentaerythritol triallyl ether, and pentaerythritol tetraallyl ether, and combinations there-

of; polyallyl ethers of trimethylolpropane such as trimethylolpropane diallyl ether, trimethylolpropane triallyl ether, and combinations thereof. Other suitable polyunsaturated compounds include divinyl glycol, divinyl benzene, and methylenebisacrylamide.

[0022] Non limiting examples of crosslinking monomers derived from ethoxylated polyols are acrylate and methacrylate esters of polyols having at least two acrylate or methacrylate ester groups, such as polyethylene glycol diacrylate, polyethylene glycol dimethacrylate, trimethylolpropane ethoxylated (15) triacrylate (TMPEO15TA) and ethoxylated (30) bisphenol A dimethacrylate (EOBDMA), and the like.

[0023] The polymer may comprise a grafted polymer or copolymer wherein one or more polyols are grafted to the polymer backbone. The polyol may comprise any polyol with a molecular weight of up to about 10000, or in the range from about 50 to about 5000, or from about 50 to about 1000, that contains 2 or more hydroxyl groups, or from 2 to about 6 hydroxyl groups, or from 2 to about 4 hydroxyl groups. Examples of the polyols that may be used include polyalkylene glycol, polyethylene glycol, polypropylene glycol, ethylene glycol, propylene glycol, glycerol, 1,3-propanediol, starch, pentaerythritol, trimethylolpropane, sorbitol, sucrose, xylitolglucose, resorcinol, catechol, pyrogallol, glycollated ureas, 1,4-cyclohexanediol, diethanolamine, triethanolamine, or a mixture of two or more thereof. In one embodiment it is preferred that at least 50 wt.% of the polyols be glycerol.

[0024] The number of structural units derived from itaconic acid, or anhydride or salt thereof, and/or the one or more comonomers referred to above in the polymer backbone that may be grafted with a polyol may be up to about 30% of the structural units, or from about 1% to about 30%, or from about 1% to about 20% of the structural units may be grafted with a polyol. The num-

ber of structural units derived from itaconic acid, or anhydride or salt thereof, in the polymer backbone that may be grafted with a polyol, may be up to about 30% of the structural units, or from about 1% to about 30%, or from about 1% to about 20% of the structural units may be grafted with a polyol.

[0025] The monomers in the improved polymers may be in the form of salts, such as, for example, sodium, potassium or ammonium salts and alkylated ammonium salts such as triethyl ammonium salt, and alkylated hydroxyl ammonium salts such as triethanol ammonium salt, and the like.

[0026] In certain instances when including AMPS type monomers, it may be desirable to replace a minor portion of the monomers in the improved polymer with AMPS monomer. In such instances, the AMPS can be present from about 0.1 to about 10 mole%, or about 0.5 to about 5 mole%, or about 1 to about 2.5 mole% of the copolymer and/or terpolymer, in which case the other co-monomers in the improved polymer will be in the range of about 90 to about 99.9 mole%, or about 95 to about 99.5 mole%, or about 97.5 to about 99% of the copolymer and/or terpolymer.

[0027] The improved polymers are free of, or substantially free of moieties of tri-substituted vinyl monomer isomers of itaconic acid, such as citriconic acid and mesaconic acid. By “substantially free of moieties of tri-substituted vinyl monomer isomers,” it is meant that there is an insufficient amount of the isomer moieties present in the improved polymer to effect the efficacy of the improved polymer, such as, for example, less than 0.5 mole %, or 0.1 mole %, or less than 0.05 mole %, or less than 0.01 mole %, based on the number of monomer units in the improved polymer.

[0028] Further, the improved polymer solution will include less than 0.5% w/w unreacted monomer and co-monomer based on the total weight of the polymer present in the solution, or less than

0.25% w/w, or free or substantially free of unreacted monomer and co-monomer. Here again, by “substantially free of unreacted monomer” it is meant that there is an insufficient amount of unreacted monomer present in the improved polymer solution to affect the efficacy of the solution, such as, for example, less than 0.5 mole %, or 0.1% w/w, or less than 0.05% w/w, or less than 0.01% w/w, or less than 0.001% w/w, based on the weight of the improved polymer in the solution, or from less than 2.5 or 2.0 wt%, or 1 wt%, or less than 0.5 wt%, or less than 0.1 wt.%.

[0029] The improved polymers can have number average molecular weights (M_n) of from about 500 to 10,000,000, preferably from about 1000 to 1,000,000, more preferably from about 2500 to about 500,000. In some embodiments the M_n of the improved polymers can be from about 500 to about 100,000 or 1000 to about 50,000. Likewise, the improved polymer can have a polydispersity of from about 1 to 60, more preferably 1 to 30, or 1 to 20 or 10, or 8.

[0030] The improved polymers can be prepared by polymerizing itaconic acid on its own, or a major amount of itaconic acid monomer with at least one comonomer. The polymerization process can provide homogenous, substantially homogenous, random or block polymers and copolymers and/ or crosslinked polymers.

[0031] Block copolymer are defined by the art as polymers derived from two or more different monomers in which multiple sequences, or blocks, of the same monomer alternate in series with the different monomer blocks. Block copolymers can contain two blocks (di-block), three blocks (tri-block), or more than three blocks (multi-block). Block copolymers can be alternating copolymers with the two or more different monomers along the polymer backbone at regularly alternating intervals. There are also periodic copolymers in which the two or more monomers are arranged in a regularly

repeating sequence, and statistical copolymers in which the sequence of the two or more different monomers repeat based on a statistical rule. Preferably, the block copolymer created according to the process of the invention is an alternating multi-block copolymer.

[0032] In one aspect of the invention, the improved polymers of the invention can be synthesized by free radical polymerization of the monomer mixture described above. The polymers can be prepared via solution, dispersion, precipitation, mass or emulsion (or inverse emulsion) polymerization techniques that are well-known in the polymer art. In one aspect the present polymers are prepared by solution polymerization in solvents, preferably in water, isopropyl alcohol and their mixtures thereof.

[0033] The polymerization process is completed in an aqueous medium in the presence of a polymerization initiator and at lower temperatures than taught in the prior art. In general, the comonomers and the initiator are added separately from the itaconic acid, but they can also be added simultaneously with the itaconic acid. Certain co-monomers, such as acrylic acid, methacrylic acid and AMPS copolymerize in essentially the same manner with itaconic acid, and may therefore be interchanged or mixed in the process to give products with essentially the same molecular weight and improved metal ion-binding characteristics for a copolymer of given AMPS or (meth)acrylic acid/itaconic acid mole ratio.

[0034] The process can include a pre-neutralization step in which the pH of the polymerization solution is neutralized with a neutralizer, (i.e. a source of sodium, potassium or ammonium and alkylated ammonium such as triethyl ammonium, and alkylated hydroxyl ammonium such as triethanol ammonium, and the like) to a pH of greater than about 1.8, or greater than about 2 or 3. The closer the pH to neutral (i.e., 7) the less corrosive the polymer solu-

tion will be. However, the greater the amount of neutralization the more likely it is for the itaconic acid to isomerize. Thus, the neutralizer is added in an amount suitable to achieve a pH of greater than 1.8 but less than the critical threshold at which itaconic acid will isomerize. Generally, the neutralizer can be added during the pre-neutralization step at a dosage to neutralize no more than 20 mole % of the carboxylic acid groups from the itaconic acid monomers. Preferably, the neutralizer can be added during the pre-neutralization step at a dosage to neutralize no more than 20 mole %, 15 mole %, or 10 mole % of the total carboxylic acid groups from all monomers, more preferably no more than 5 mole %. In some embodiments, the neutralizer can be added during the pre-neutralization step at a dosage to neutralize from about 0.01 to about 20 mole % of the carboxylic acid groups from all monomers, more preferably from about 0.1 to about 15 mole %, or from about 0.5 to about 10 mole %, or even 1 to about 5 mole % of the carboxylic acid groups from all monomers.

[0035] The neutralizer can be an alkali metal base, ammonium, and/or amine base. Alkali metal bases suitable for the neutralization include sodium hydroxide, potassium hydroxide and lithium hydroxide, while suitable ammonium and amine bases include ammonia, ammonium hydroxide, mono-, di- and trialkyl amines having 1 to 5 carbon atoms in each alkyl group, pyridine, morpholine and lutidine. The neutralizer can also be a base with carboxylic acid functionality, although it is preferred that such a neutralizer has less than 25 mole % carboxylic acid functionality. Examples of neutralizers having carboxylic acid functionality include, but are not limited to, amino acids, peptides, polypeptides, and their derivatives. The amino acid can be chosen from alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine,

isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, and valine.

[0036] Any water-soluble, free-radical initiator may be used as the polymerization initiator of this process. Suitable initiators include persulfates such as sodium and potassium persulfate as well as redox systems. Other initiators, such as hydrogen peroxide, benzoyl peroxide, acetyl peroxide, and lauryl peroxide, cumene hydroperoxide and t-butyl hydroperoxide; organic peracids, such as peracetic acid; and oil and water soluble free radical producing agents, such as 2,2'-azobisisobutyronitrile, and the like, and mixtures thereof can also be used in combination with water soluble initiators. Suitable reducers for the redox system include sulfur compounds, such as, for example, the sodium salt of hydroxymethanesulfinic acid, a mixture of a disodium salt of 2-hydroxy-2-sulfinatoacetic acid and sodium sulfite, Brüggolit™ FF6 and FF7, sodium sulfite, sodium disulfite, sodium thiosulfate, and acetone-bisulfite adduct. A typical redox system can include, consist essentially of, or consist of, for example, sodium persulfate type oxidizers with sodium bisulfite type reducers, such as Brüggolit™ FF6. In one embodiment, the reaction mixture is free of metal promoters, such as copper and the like.

[0037] Optionally, other polymerization additives and processing aids which are well known in the solution polymerization art, such as, chain transfer agents, solvents, emulsifiers, processing aids, defoamers, buffering agents, chelating agents, inorganic electrolytes, polymeric stabilizers, biocides, and pH adjusting agents can be included in the polymerization system.

[0038] The polymerization can be carried in a variety of solvents, such as alcohols, ethers, esters, aromatic solvents, glycols, glycol ethers, glycerol and glycol esters. Preferred solvents include ethyl alcohol, isopropyl alcohol, t-butyl alcohol, ethyl acetate, me-

thyl acetate, butyl acetate, benzene, toluene, and methylene chloride. These solvents can be used also in combination with hydrocarbon solvents such as hexane, cyclohexane, mineral spirits, and the like. Glycerol, isopropyl alcohol, water, or a mixture of two or more thereof are preferred.

[0039] The polymerization initiator should be present in an amount of less than about 5 mole % based on the total amount of the monomers, such as from about 0.01 to about 5 mole %, or 0.1 to about 4.95 mole %, and even about 1 to about 4.9 mole % based on the total amount of the monomers. All or at least half of the initiator can be added separately from the itaconic acid monomer. In one embodiment, the initiator can be added essentially continuously throughout the polymerization period. The initiator can also be added in discreet amounts at various times through the polymerization period. Preferably, from about 0.5 to 5 mole % of the initiator charge is dissolved along with the itaconic acid in the aqueous medium and the remainder of the initiator is then introduced, preferably as an aqueous solution, over the polymerization period or with the co-monomers. The concentration of the initiator in the aqueous addition solution is normally from about 0.5 to 10 weight%.

[0040] The temperature and duration of the polymerization are influential in determining the nature of the resulting copolymer. The polymerization is therefore limited to temperatures of from about 55 to 90°C, or from 60 to 85°C, or even from 60 to 80°C. The polymerization period can be sustained at from about 2 to about 8, 12, or 16 hours. The final polymerization solution is generally maintained at the polymerization temperature until reaction is completed following the completion of the co-monomers and initiator addition period.

[0041] By the selection of the above reaction parameters within the specified ranges, homogeneous or substantially homogeneous

polymers, or random or block copolymers and/or terpolymers of itaconic acid, (meth)acrylic acid and/or AMPS can be prepared with number average molecular weights (M_n) of from about 500 to 100,000, preferably from about 1000 to 50,000, more preferably 1000 to 10,000.

[0042] Importantly, the improved polymer, copolymers, terpolymers and/or crosslinked polymers produced according to the above process will be free of or substantially free of moieties of tri-substituted vinyl monomer isomers of itaconic acid, such as citri-conic acid and mesaconic acid. Further, the resulting polymer solution will include less than 0.5% w/w unreacted monomer based on the total weight of the polymer present in the solution, or less than 0.25% w/w, or free or substantially free of unreacted monomer.

[0043] In addition, the polymer solution will be transparent or substantially transparent. Transparency of a solution can be measured in terms of the turbidity of the solution; that is the cloudiness or haziness of the solution. Turbidity is measured on a nephelometer in nephelometric turbidity units ("NTU"). By transparent it is meant that the solution has a turbidity of less than 5 NTUs. Substantially transparent means the polymer solution has a turbidity of between about 5 and 100 NTUs, or more preferably 5 and 50 NTUs, 5 to 25 NTUs, or 5 to 15 NTUs.

[0044] Preferred embodiments of the instant process include those in which from about 30 to 40 mole % acrylic acid is copolymerized with from about 60 to 70 mole % itaconic acid. In an especially preferred process, about 30 to 40 mole % acrylic acid, 1 to 2 mole % sodium persulfate and 1 to 2 mole % Brüggolit™ FF6 are added separately over a period of about 3 to 5 hours to an aqueous solution of about 60 to 70 mole % itaconic acid at a temperature of

between about 60° to 80°C, and the polymerization solution is held at temperature for an additional 4 hours following the addition.

[0045] The improved polymers consisting essentially of from about 30 to 40 mole % co-monomer and from about 60 to 70 mole % itaconic acid derived monomer units, and having a number average molecular weight of from about 500 to 100,000, preferably from about 1000 to 50,000, more preferably 1000 to 10,000. The copolymer will normally be added to aqueous systems. The final polymerization solution, as such, diluted or concentrated as desired, will generally be used without isolation of the copolymer product.

[0046] Liquid polymers can also be dried using various drying techniques as known in the prior art [Handbook of Industrial Drying, by Arun S. Mujumdar, Third Edition, 2007]. Some commonly used polymer dryers are rotary dryer, flash dryer, spray dryer, fluidized bed dryer, vibrated fluidized bed dryer, contact fluid-bed dryer, paddle dryer, plate dryer, and DRT spiral dryer.

[0047] Evaluation of these improved polymers has shown them to be superior to the itaconic acid polymers of the prior art.

[0048] The improved polymers of the present invention are especially useful in the prevention of stains on the surface of hydroxyapatite surface, such as teeth. In such use, the copolymer is normally added to an oral care formulation in an effective amount to bring the effects to the oral care formulation, normally at a level from about 0.01 to 20 weight % active, and preferably from about 0.05 to 10 weight %, or about 0.1 to about 5 weight %, or about 0.25 to about 2.5 weight percent. Evaluation of these improved polymers has shown them to be superior to the itaconic acid polymers of the prior art.

[0049] The improved polymers can therefore be employed in a method of preventing stains on a hydroxyapatite surface, such as teeth. The method can comprise adding to an oral care formulation

the improved polymers or solutions thereof. Preferred oral care formulations include dentifrice or gel and mouthwash (e.g., spray, rinse, solutions and suspensions). Other types of oral care formulations include denture adhesives, denture cleaning products, dental composites, tooth whiteners, tooth varnishes, lozenges and chewing gum.

[0050] In certain forms of this invention, the oral care formulation may be substantially solid or pasty in character, such as tooth powder, a dental tablet, toothpaste, gel or dental cream. The vehicle of such solid or pasty oral preparations generally contains a polishing material. Examples of polishing materials are water-insoluble sodium metaphosphate, potassium metaphosphate, tricalcium phosphate, dehydrated calcium phosphate, anhydrous dicalcium phosphate, calcium pyrophosphate, magnesium orthophosphate, trimagnesium phosphate, calcium carbonate, sodium bicarbonate, aluminum silicate, zirconium silicate, silica, bentonite, and mixtures thereof. Other suitable polishing materials include the particulate thermosetting resins described in U.S. Pat. No. 3,070,510 such as formaldehydes of melamine, phenol, and urea, and cross-linked polyepoxides and polyesters. Preferred polishing materials include crystalline silica having particle size of up to about 5 microns, a mean particle size of up to about 1.1 microns, and a surface area of up to about 50,000 cm²/gm, silica gel or colloidal silica, and complex amorphous alkali metal aluminosilicate.

[0051] When visually clear gels are employed, a polishing agent of colloidal silica and alkali metal aluminosilicate complexes are particularly useful since they have refractive indices close to the refractive indices of the liquid gelling agent.

[0052] The linear, molecularly dehydrated polyphosphate salts operative herein as abrasive dental additives are well known, being generally employed in the form of their wholly or partially neutral-

ized water soluble alkali metal or ammonium salts and mixtures thereof. Representative examples include sodium hexametaphosphate, sodium tripolyphosphate, disodium diacid, trisodium monoacid, and tetrasodium pyrophosphates, and the like. Linear polyphosphates correspond to $(\text{NaPO}_3)_n$ where n is about 2 to about 125. They are generally employed in the instant oral care compositions in approximate weight amounts of 0.1 to 7%, preferably 1 to 5%.

[0053] The polishing material or dental abrasive is generally present in the solid or pasty compositions in weight concentrations of about 1% to about 99% preferably, it is present in amounts ranging from about 3 or 5% to about 75% in toothpaste, and from about 70% to about 99% in toothpowder.

[0054] Toothpastes, creams and gels typically contain a natural or synthetic thickener or gelling agent in proportions of about 0.1 to about 15, preferably about 0.5 to about 10 weight percent and even from 1 to 5 weight percent. A suitable thickener can be cellulosic polymers, natural gums, semi-synthetic gum, synthetic hectorite, silica, a synthetic colloidal magnesium, alkali metal silicate complex clay, and carboxyvinyl polymer or polyacrylic acid of intermediate molecular weight.

[0055] The oral care compositions of this invention can contain a variety of optional conventional oral ingredients. Such optional ingredients include surface active agents, flavoring agents, sweetening agents, binding agents, coloring agents, humectants, and pigments.

[0056] A preferred optional ingredient is a surface acting agent. Suitable surfactants are those which are reasonably stable and form suds throughout a wide pH range, i.e., non-soap anionic, cationic, zwitterionic and amphoteric organic synthetic detergents. Surface acting agents of these types, are described more fully in Agricola et al U.S. Pat. Nos. 3,959,458 and in Haefele 3,937,807.

[0057] Flavoring agents can also be added to the instant compositions. Suitable flavoring agents include oil of wintergreen, oil of peppermint, oil of spearmint, oil of sassafras, menthol, cinnamon, and oil of clove and other volatile oils. Sweetening agents which can be used include sorbitol, glycerin, saccharin, dextrose, levulose, aspartame, D-tryptophan, dihydrochalcones, acesulfame, xylitol, mannitol and sodium cyclamate and the like. Flavoring agents are generally used in the compositions at levels of from about 0.4% to about 10% by weight and sweetening agents at levels of from about 0.1% to about 65% or 75 % by weight.

[0058] The oral care formulations can also include coloring agents. Suitable coloring agents can include, for example, titanium dioxide, FD&C colors and any colorant used for food and pharmaceutical products and the like.

[0059] Binders can also be used with the toothpastes of the present inventions. Such binders include, for example, cellulosic polymers, xanthan gum, carrageenan (Irish moss), natural and semi-synthetic gums, and carboxyvinyl polymers or polyacrylic acids of intermediate molecular weight, and the like. These binders are generally present at a level of from about 0.1% to 5%.

[0060] Another optional component of the compositions herein is a humectant. The humectant serves to keep the toothpaste compositions from hardening upon exposure to air and in mouthwashes, give a moist feel to the mouth. Certain humectants can also impart desirable sweetness or flavor to mouthwash and toothpaste compositions. The humectant, on a pure humectant basis, generally comprises from about 0% to 70%, preferably from about 5% to 55%, by weight of the compositions herein.

[0061] Suitable humectants for use in this invention include edible polyhydric alcohols such as glycerine, sorbitol, xylitol, poly-

ethylene glycol, propylene glycol and other glycols. Sorbitol is frequently employed as a 70% aqueous solution.

[0062] The mouthwashes herein may also contain ethanol in an amount of from about 0 to about 30%, preferably 5 to 25%, as a germicide.

[0063] The pH of the compositions herein is in the range of 3 to 10, preferably from 4 to 8. The pH is preferably achieved through a proper balancing of the ingredients listed above or by the addition of an alkaline or acidic agent.

[0064] Other optional ingredients can include film forming polymers, such as polyvinyl acetate, acrylics, cellulose and the like, bleaches, including peroxide, fixatives, and dental composite ingredients.

[0065] Water employed in the preparation of commercially suitable oral care compositions should preferably be of low ion content and free of organic impurities. Water comprises from about 2% to about 95%, preferably from about 20% to about 95% of the compositions of this invention. When in the form of toothpastes, the amount of water is preferably from about 2% to about 45%, while mouthwashes preferably contain from about 45% to about 95%.

[0066] The amount of each chemical component described is presented exclusive of any solvent or diluent, which may be customarily present in the commercial material, that is, on an active chemical basis, unless otherwise indicated. However, unless otherwise indicated, each chemical or composition referred to herein should be interpreted as being a commercial grade material which may contain the isomers, by-products, derivatives, and other such materials which are normally understood to be present in the commercial grade.

[0067] It is known that some of the materials described above may interact in the final formulation, so that the components of the

final formulation may be different from those that are initially added. For instance, metal ions (of, e.g., a detergent) can migrate to other acidic or anionic sites of other molecules. The products formed thereby, including the products formed upon employing the composition of the present invention in its intended use, may not be susceptible of easy description. Nevertheless, all such modifications and reaction products are included within the scope of the present invention; the present invention encompasses the composition prepared by admixing the components described above.

EXAMPLES

Test Methods

Viscosity

[0068] Brookfield rotating spindle method (all viscosity measurements reported herein are conducted by the Brookfield method whether mentioned or not): The viscosity measurements are calculated in mPa·s, employing a Brookfield rotating spindle viscometer, Model RVT (Brookfield Engineering Laboratories, Inc.), at about 20 revolutions per minute (rpm), at ambient room temperature of about 20 to 25°C (hereafter referred to as viscosity). Spindle sizes are selected in accordance with the standard operating recommendations from the manufacturer. Generally, spindle sizes are selected as follows:

[0069]

Spindle Size No.	Viscosity Range (mPa·s)
1	1 - 50
2	500 - 1,000
3	1,000 - 5,000
4	5,000 - 10,000
5	10,000 - 20,000
6	20,000 - 50,000
7	>50,000

[0070] The spindle size recommendations are for illustrative purposes only. The artisan of ordinary skill in the art will select a spindle size appropriate for the system to be measured.

Turbidity Testing

[0071] The turbidity of a composition containing a polymer of the invention is determined in Nephelometric Turbidity Units (NTU) employing a Nephelometric turbidity meter with distilled water (NTU = 0) as the standard.

Molecular Weight Determination

[0072] The weight average molecular weights referenced herein are measured by GPC using a Waters Model 515 pump, Waters Model 717 WISP autosampler with Waters Model 2410 Refractive Index @ 40°C. Approximately 0.01 g polymer sample is dissolved in 10 ml of 97.5% 0.1M Sodium Nitrate with 2.5% tetrahydrofuran (THF). The test sample solution is gently shaken for about two hours and filtered by passing the sample solution through a 0.45 µm PTFE disposable disc filter. The chromatographic conditions are: Mobile phase: 97.5% 0.1M Sodium Nitrate/ 2.5% THF (pH=10),

0.7 ml/min. Sample size: 100 μ l Column set: TOSOH Guard + 2 x TSKgel GMPWxl (13u), 300 x 7.8 mm, @ 35°C. Waters Empower Pro LC/GPC software is used to analyze the results and to calculate M_w of the polymers of the invention.

[0073] The molecular weight calibration curve was established with polyacrylic acid standards contained in the "PSS-PAAKIT" from *Polymer Standards Service-USA*. Acrylic acid with MW=94 Daltons was added to one standard. The calibration curve covered an M_p range from 94 to 1.10×10^6 Daltons.

^1H NMR

[0074] The ^1H NMR spectra referenced herein are measured by dissolving the samples in D_2O solvent in 5mm NMR tubes and observed by ^1H NMR on the Bruker AV500.

Residual Monomers

[0075] Residual monomers such as, itaconic acid, acrylic acid and AMPS are measured by HPLC using a Varian 5020 with UV detector, Spectra-Physics 4100 data analyzer and column C-18 modified silica such as Phenomenex Jupiter 5u C-18 300A, 4.6 mm I.D. x 25 cm at 20°C. Mobile phase is the solution of 0.01M KH_2PO_4 with flow rate 1 ml/minute. Monomer detection limit is < 5 ppm.

Calcium Binding Capacity:

[0076] The calcium chelating capacity of the polymers is measured using Thermo Orion Calcium Ion Selective Electrode (ISE) connected to an Orion Start Plus Meter. The instrument is calibrated using four standard(Calcium chloride (CaCl_2) solutions with concentrations of 0.0001 M, 0.001 M, 0.01 M and 0.1 M. 1% chelator solution is prepared in DI water and its pH is adjusted to desired value using NaOH solution.

[0077] The following procedure is used for a typical sample titration:

- Burette is filled with 1% chelator solution.

- In a 250 mL beaker containing a magnetic stir bar, 100 mL of 0.01 M CaCl₂ solution is taken. 2 mL of Ionic Strength Adjuster (ISA) is added.
- The ISE and reference electrodes are rinsed with distilled water, wiped and placed in the solution.
- The chelator solution is titrated from the burette and the Ca²⁺ concentration is monitored in the Orion Star Plus meter.
- The chelator solution is added gradually until the meter shows 0.00 M concentration of Ca²⁺.
- The end point of the titration is used to calculate the Calcium binding capacity of the polymer in mg of CaCO₃/g of polymer using the following equation:

$$\text{mg of CaCO}_3/\text{g of polymer} = \frac{0.100087 * M}{0.01} * 100 * \frac{1000}{BR}$$

where M = starting molarity of CaCl₂ solution and BR = Burette reading, mL at the end point of the titration.

Abbreviations

[0078] The following abbreviations and trade names are utilized in the examples.

ABBREVIATIONS and Trade Names

Abbreviation	Chemical Name
IA	Itaconic acid
AA	Acrylic acid
AMPSTM Mono- mer	2-acrylamido-2-methylpropane sulfonic acid (Lubrizol Advanced Materials, Inc.) sodium salt
SPS	Sodium persulfate
FF6	Reducer (mixture of a disodium salt of 2-hydroxy-2-sulfinatoacetic acid and sodium sulfite) available from Brüggolit
BA	Butyl acrylate

HEMA Phosphate	Phosphate containing monomer, Sipomer PAM-4000, Rhodia
HEMA	Hydroxyethyl methacrylate
NaOH	Sodium hydroxide
Glycerol	Glycerol
PEGDA	Polyethylene glycol diacrylate (mw -575)
PAA	Low molecular weight polyacrylic acid (Noverite™ K 7058, Lubrizol Advanced Materials, Inc)
HAP Disc	Dense (sintered) Hydroxyapatite (HAP) disc and Calcium deficient (porous) HAP disc from HiMed, Inc.

Sample 1: Polyitaconic acid

[0079] Into an agitator equipped reactor containing 250 grams of deionized water (D.I.) and 250 grams of itaconic acid are added under nitrogen atmosphere and mixed at 300 rpms. The contents of the reactor are heated to about 60°C with mixing agitation (300 rpm) under a nitrogen atmosphere for 30 minutes. When the contents of the reactor reaches a temperature of approximately 60°C, 30 grams of FF6 solution (0.084% aqueous solution weight/weight) and 26.25 gram sodium persulfate solution (38 percent aqueous solution weight/weight) are injected into the heated IA solution in 10 minutes interval. After 30 minutes, the reaction temperature is raised to 80 to 85°C. When the contents of the reactor reaches a temperature of approximately 80 to 85°C, 28.5 percent sodium persulfate solution (aqueous solution weight/weight) is also metered at 0.44 mL/minute into the reaction mixture for 75 minutes. The temperature of the reaction is maintained at about 80 to 85°C for an additional four hours to complete the polymerization. The resulting polyitaconic acid product is cooled to room temperature and adjust-

ed the product pH from < 1.0 to 2.5 with 50% NaOH before discharging from the reactor.

Samples 2-4: Polyitaconic acid

[0080] Sample 1 is repeated to make Samples 2-4 with pre-neutralized itaconic acid as mentioned in Table 1 to investigate the effect of neutralization on IA isomerization as well as its conversion. A neutralizing solution of 50% NaOH at different percent based on the acid groups of the IA monomer is added along with IA and is referred to as the percent degree of neutralization (%DN). Samples 2-4 contain 5, 10 and 20% DN neutralizing solution respectively.

Comparative Sample I

[0081] A polyitaconic acid polymer is prepared in water using the procedure of Example I in US Patent No. 7,910,676 at 50% DN using 70% tBHP initiator at reflux condition.

Example 1

[0082] Polymer Samples 1 to 4 and Comparative Sample I are characterized for %total solid, pH, product viscosity, conversion (by HPLC), and IA isomerization by ¹H NMR. The results are shown in Table 1 below. A significant amount of citraconic acid (IA isomer) is noticed by the presence of cis- and trans- CH₃-peak at 2.1 and 1.97 ppm and cis- and trans- methine -CH- peak at 5.8 and 6.55 ppm as shown in Figure 1 in the Comparative Sample I as well as poor IA conversion. Samples 1-4 are markedly free of IA isomer with better conversion.

Table 1: Polyitaconic acid made with different pre-neutralized conditions (%DN)

Test	Sample				
	1	2	3	4	Comp. I
%DN	0	5	10	20	50
Temp °C	85	85	85	85	100
pH	2.6	2.21	2.73	3.5	4.85
% Total Solids	39.5	42.3	49.7	37.3	51

Viscosity (cP)	71	76	1340	56	540
Residual Monomer (ppm)	1160	18500	4050	20800	45600
Mn	1917	1692	2195	1564	1827
PDI	2.43	2.58	3.31	2.59	1.44
Isomerization by ¹ H NMR	none	none	none	trace	significant

Sample 5: 90/10 Mole % Itaconic acid / acrylic acid copolymer

[0083] Into an agitator equipped reactor containing 225 grams of deionized water (D.I.) and 235.5 grams of itaconic acid are added under nitrogen atmosphere and mixed at 300 rpms. The contents of the reactor are heated to about 60°C with mixing agitation (300 rpm) under a nitrogen atmosphere for 30 minutes. When the contents of the reactor reaches a temperature of approximately 60°C, 30 grams of FF6 solution (0.084% aqueous solution weight/weight) and 26.25 gram sodium persulfate solution (38 percent aqueous solution weight/weight) are injected into the heated IA solution in 10 minutes interval. After 30 minutes, the reaction temperature is raised to 85°C. When the contents of the reactor reaches a temperature of approximately 85°C, 28.5 percent sodium persulfate solution (aqueous solution weight/weight) is also metered at 0.44 mL/minute into the reaction mixture for 75 minutes. Concurrently, the comonomer solution, made from 14.5 grams AA monomer mixed with 12.5 grams of water, is also gradually metered (0.43 g/min.) into the reactor over a period of about 60 minutes to react with IA. The temperature of the reaction is maintained at about 85°C for an additional four hours to complete the polymerization. The resulting copolymer of itaconic acid and acrylic acid product is cooled to room temperature and adjusted the product pH to 2.5 with 50% NaOH before discharging from the reactor.

[0084]

Samples 6-12: Itaconic acid / acrylic acid copolymers

[0085] Polymers 6 through 12 are also synthesized as set forth in Sample 5. A neutralizing solution of 50% NaOH at 5 percent based on the acid groups of the total monomers (5% DN) is added along with IA in Samples 11 and 12. The monomer components for these Samples are set forth in Table 2 below.

Comparative Sample II

[0086] A copolymer of 90/10 mole % of IA/ AA is prepared using the procedure of Example 2B in US Patent No. 4,485,223 at reflux condition with about 20 wt% (0.1 mole %) initiator.

Example 2

[0087] Polymer Samples 6 to 12 and Comparative Sample II are characterized for %total solid, pH, product viscosity, conversion and IA isomerization by ^1H NMR. The results are shown in Table 2 below. The combination of both high initiator level and high temperature (reflux) conditions in the preparation of Comparative Sample II causes the initiator to decompose quickly, resulting in 1) a polymer solution having a dark color and undesirable sulfur odor, with oxidized and sulfurized itaconic acid impurities along with unreacted monomers (Figure 2), and 2) poor performance for chlorine retention. Surprisingly, the combination of both lower temperature (85°C) and redox initiator (oxidizer-SPS and reducer-FF6) package employed in Samples 6 to 12 yields cosmetically acceptable color and odor, and relatively pure copolymer products (Figure 3) with desirable Mn and other properties. Furthermore, the use of less than 5% equivalent pre-neutralization (referred to as DN) eliminates the hazardous corrosiveness issue due to the low pH < 1 of the final product and subsequently makes the process suitable for commercial manufacturing options.

Table 2: IA-AA copolymers

Test	Sample									
	5	6	7	8	9	10	11	11a	12	Comp II
Mole % IA/AA	90/10	80/20	70/30	60/40	50/50	30/70	60/40	60/40	70/30	90/10
Wt% IA/AA	94.2/5.8	88/12	80.8/19.2	73/27	64.8/35.6	43.6/56.4	73/27	73/27	80.8/19.2	94.2/5.8
Temp °C	85	85	85	85	85	85	85	75	85	102 (reflux)
%DN	0	0	0	0	0	0	5	8.4	5	0
pH	2.5	2.51	2.5	2.53	2.52	2.5	2.75	2.72	2.74	<1.0
% Total Solids	47	42.3	43.2	43.4	44.7	37.8	49	47.5	46.3	49.5
Viscosity (cP)	198	137	179	268	334	250	712	1530	455	78
Total	1455	4154	182	44	34	17	71	17	45	14870
Residual Monomers (ppm)										
Mn	2474	2339	3679	4087	4275	5350	4048	6498	2138	666
PDI	2.1	2.09	2	3.24	6.26	9.14	2.7	4.4	2.4	3.05
NTU	2.11	0.79	0.55	0.94	1.29	0.62	3	1.3	2	50
Color (Gardner Scale)	10	9	8	5	6	4	6	10	8	16

Samples 13 – 22: IA Copolymers and Terpolymers with AMPS**Monomer**

[0088] Polymers 13 through 22 are also synthesized as set forth in Sample 5 (e.g., at a reaction temperature of 85°C and with 0% DN) except a sodium salt of AMPS monomer is used in place of AA or in combination with AA. The monomer components for these Samples are set forth in Table 3 below.

[0089]**Table 3**

Sample	Mole % IA/AA/AMPS	Wt% IA/AA/AMPS	pH	% Total Solids	Viscosity (cP)	Total residual Monomers (ppm)	Mn	PDI	NTU	Color (Gardner Scale)
13	90/0/10	83.6/0/16.4	2.5	41.1	63	9410	2166	2.05	1.23	9
14	80/0/20	69.4/0/30.6	2.5	40.1	60	30	1398	2	0.76	8
15	70/0/30	57/0/43	2.51	41.3	84	30	3071	2.79	0.75	6
16	60/0/40	46/0/54	2.52	40.4	80	18	2988	3.51	0.49	5
17	50/0/50	36.2/0/63.8	2.53	39.3	82	12	3627	4.14	0.4	4
18	30/0/70	19.6/0/80.4	2.52	28.8	67	80	3210	5.05	0.4	5
19	60/30/10	63.5/17.5/19	2.52	46.9	380	45	3562	4.79	1.22	6
20	60/25/15	60/13.8/26.2	2.53	46	314	23	3733	5.02	1.15	6
21	60/20/20	56.4/10.4/33.2	2.53	39.9	78	15	2922	3.6	1.09	6
22	60/10/30	52.6/4.9/46.5	2.52	39.7	78	159	2566	4.15	0.61	5
23	10/0/90	16.8/0.0/83.2	2.6	46.0	3008	206	7989	9.66	NA	1

Sample 24: Grafted IA Crosslinked copolymer:

[0090] Itaconic acid (120.25g, 0.925mole), glycerol (46.05g, 0.5mole) and 150g water are placed in a 500ml reactor and heated to 70°C under nitrogen atmosphere, 2g sodium persulfate is added. Heating is continued to 75°C when a premix of polyethyleneglycol diacrylate (Mw: ~575, 2.59g, 5mmole), acrylic acid (10.8g, 0.15mole) and 15g de-mineralized water are metered via a syringe over 120 minutes, followed by a 5g demineralized (DM) water flush. 30 minutes into the premix addition another stream of initiator of 4g SPS in 12g DM water is metered in over 4 hours, followed by a 5g DM water flush. The reaction is heated at 75°C for another 30 minutes before cooling to 60°C, when a redox of 0.6g SPS in 4g DM

water is followed by 0.6g Burgolit FF-6 in 10g DM water. The reaction is then cooled down and poured into a jar.

Sample 25: Grafted IA Crosslinked Copolymer:

[0091] Itaconic acid (120.25g, 0.925mole), glycerol (9.21g, 0.1mole) and 150g water are placed in a 500ml reactor and heated to 70°C under nitrogen atmosphere, 2g sodium persulfate is added. Heating is continued to 75°C when a premix of polyethyleneglycol diacrylate (Mw: ~575, 2.59g, 5mmole), acrylic acid (10.8g, 0.15mole) and 15g DM water are metered via a syringe over 120 minutes, followed by 5g DM water flush. 30 minutes into the premix addition another stream of initiator of 4g SPS in 12g DM water is metered in 4 hours, followed by 5g DM water flush. The reaction was heated at 75°C for another 30 minutes before cooling to 60°C when a redox of 0.6g SPS in 4g DM water is followed by 0.6g Burgolit™ FF-6 in 10g DM water. The reaction is then cooled down and poured into a jar.

Sample 26: Grafted IA Crosslinked Copolymer

[0092] Itaconic acid (117g, 0.9mole), glycerol (9.21g, 0.1mole) and 120g water are placed in a 500ml reactor, 2g sodium persulfate is added and the mixture is heated to 85°C under nitrogen atmosphere when a premix of polyethyleneglycol diacrylate (Mw: ~575, 2.59g, 5mmole), acrylic acid (14.4g, 0.2mole) and 10g DM water are metered via a syringe over 120 minutes, followed by 5g DM water flush. 30 minutes into the premix addition another stream of initiator of 4g SPS in 12g DM water is metered in 4 hours, followed by 5g DM water flush. The reaction is heated at 75°C for another 30 minutes before cooling to 60°C when a redox of 0.6g SPS in 4g DM water is followed by 0.6g Burgolit™ FF-6 in 10g DM water. The reaction is then cooled down and poured into a jar.

[0093]

Sample 27: Grafted IA Crosslinked Copolymer

[0094] Itaconic acid (117g, 0.9mole), glycerol (9.21g, 0.1mole), 4.7g sodium hypophosphite and 120g water are placed in a 500ml reactor, 2g sodium persulfate is added. The mixture is heated to 85°C under nitrogen when a premix of polyethyleneglycol diacrylate (Mw: ~575, 2.59g, 5mmole), acrylic acid (14.4g, 0.2mole) and 10g DM water are metered via a syringe over 120 minutes, followed by 5g DM water flush. 30 minutes into the premix addition another stream of initiator of 4g SPS in 12g DM water is metered in 4 hours, followed by 5g DM water flush. The reaction was heated at 75°C for another 30 minutes before cooling to 60°C when a redox of 0.6g SPS in 4g DM water is followed by 0.6g Burgolit™ FF-6 in 10g DM water. Some white precipitates are suspended in the reactor. The reaction is then cooled down and filtered into a jar.

Sample 28: Grafted IA Crosslinked Copolymer

[0095] Itaconic acid (117g, 0.9mole), glycerol (9.21g, 0.1mole) and 135g water are placed in a 500ml reactor. Heating to 70°C under nitrogen atmosphere, 2g sodium persulfate is added. Continue heating to 85°C when a premix of polyethyleneglycol diacrylate (Mw: ~575, 2.59g, 5mmole), acrylic acid (7.2g, 0.1mole) and butyl acrylate (12.8g, 0.1mole) are metered via a syringe in 120 minutes, followed by 5g DM water flush. 30 minutes into the premix addition another stream of initiator of 4g SPS in 12g DM water is metered in 4 hours, followed by 5g DM water flush. The reaction is heated at 75°C for another 30 minutes before cooling to 60°C when a redox of 0.6g SPS in 4g DM water is followed by 0.6g Burgolit™ FF-6 in 10g DM water. Some white precipitates are suspended in the reactor. The reaction is then cooled down and filtered into a jar.

[0096]

Sample 29: Phosphate Containing Grafted IA Copolymer

[0097] Itaconic acid (117g, 0.9mole), glycerol (9.21g, 0.1mole) and 135g water are placed in a 500ml reactor, 2g sodium persulfate is added. The mixture is heated to 80°C under nitrogen atmosphere when a premix of acrylic acid (10.8g, 0.15mole), HEMA phosphate (PAM-4000 from Rhodia, 10.5g, 0.05mole) and 10g de-mineralized water are metered via a syringe in 120 minutes, followed by 5g DM water flush. 30 minutes into the premix addition another stream of initiator of 4g SPS in 12g DM water is metered in 4 hours, followed by 5g DM water flush. The reaction was heated at 75°C for another 30 minutes before cooling to 60°C when a redox of 0.6g SPS in 4g DM water is followed by 0.6g Burgolit™ FF-6 in 10g DM water. The reaction is then cooled down and poured into a jar.

Sample 30: IA Copolymer

[0098] Itaconic acid (104g, 0.8mole) and 120g water are placed in a 500ml reactor, 2g sodium persulfate is added. The mixture is heated to 85°C under nitrogen atmosphere when a premix of acrylic acid (10.8g, 0.1mole), HEMA (13g, 0.1mole) and 10g de-mineralized water are metered via a syringe in 120 minutes, followed by 5g DM water flush. 30 minutes into the premix addition another stream of initiator of 4g SPS in 12g DM water is metered in 4 hours, followed by 5g DM water flush. The reaction was heated at 75°C for another 30 minutes before cooling to 60°C when a redox of 0.6g SPS in 4g DM water is followed by 0.6g Burgolit™ FF-6 in 10g DM water. The reaction is then cooled down and poured into a jar.

Example 3: Calcium Binding Capacity of Chelators:

[0099] The calcium binding capacities of the itaconic acid homo and copolymers and benchmark chelators are tested using the procedure mentioned above at pH 9.5 and 8.5. The results are

shown in tables 4 and 5. Higher calcium binding capacity numbers are preferred for the chelation application.

Table 4

Sample	Ca Binding, mg CaCO ₃ /g of polymer @ pH 9.5
1	229.5
5	178.5
6	215.6
7	407
8	400.3
9	203.1
10	262.6
13	208.5
14	242.9
15	205.8
16	188.0
PAA	176.4

Table 5

Samples	Ca Binding, mg CaCO ₃ /g of polymer @ pH 8.5
7	157.0
8	171.6
19	252.9
21	198.7
PAA	161.8

[00100] From the table 4, it is evident that some IA/AA copolymers have comparable or improved Ca binding capacity over the AA homopolymer at pH 9.5 and pH 8.5.

Stain Prevention Properties:

[00101] The stain prevention performance of the surface modification polymers or control samples was evaluated by a tea-staining test on sintered (dense) and porous (calcium deficient) hydroxyapatite (HAP) discs. The procedure consisted on pre-treating sintered

and porous HAP discs by immersing them in a polymer solution. Treated and un-treated HAP discs were subjected to staining with a filtered tea solution for 24 hours. The staining of the discs at different sampling time points (1, 2, and 24 hours) was assessed visually or by using spectrophotometric methods.

[00102] The stain prevention properties of the itaconic acid homo and copolymers and reference materials (control polymers, commercial toothpaste) were tested using the procedure detailed below.

[00103] Materials

- Polymers as described in the Table B1 (below)

Table B1. Polymer Solutions						
Sample	Initial pH of 3% polymer solution	Amount NaOH (18%) added (g)	Final pH of 3% polymer solution	Initial pH of 10% polymer solution	Amount NaOH (18%) added (g)	Final pH of 10% polymer solution
1	3.48	3.84	6.50	2.95	15.16	7.24
1	3.52	3.46	6.90	3.23	11.36	6.51
5	3.12	4.32	6.85	NT*	NT	NT
8	3.65	3.86	6.72	NT	NT	NT
9	2.94	4.68	6.69	2.71	16.24	6.54
21	3.03	3.00	6.98	2.83	10.02	6.47
23	3.11	6.02	6.84	3.07	19.12	6.41
24	NT	4.13	6.84	1.83	15.70	6.85
25	NT	3.86	6.53	1.86	15.57	6.85
26	2.14	5.76	6.97	1.84	18.82	6.48
27	2.28	5.56	6.82	2.00	18.62	6.49
28	2.20	5.82	6.87	1.77	19.1	6.51
Comparative II	1.90	6.00	6.80	1.56	19.90	6.47
Other Com- parative Example - Carbopol® 907	2.43	14.61	6.61	2.38	19.57	6.50
Other compar- ative Example	2.34	8.29	6.55	1.95	15.31	6.55

- Gantrez® S-

97 BF

*NT – not tested

- Hydroxyapatite (HAP) discs from HiMed, Inc.:
- Dense (sintered) HAP disc (9.5 mm dia. X 1.8 mm thick)
- Calcium deficient HAP disc (9.5 mm dia. X 1.8 mm thick)
- Nylon filter bag, FSI® 75 micron from FSI (Filters-Strainers&Installations, Inc.)
- Staining solution: Lipton® tea bag, coffee, and Diet Coke
- Sodium hydroxide from J.T.Baker, Lot # K13476

[00104] *Equipment*

- Shaker: Thermo Scientific MAXQ 4000 Shaker (Model# 4330)
- Force-air oven: Symphony™ by VWR
- pH meter: Accumet® AB15 from Fisher Scientific
- Color meter (Portable Spectrophotometer): Color-Guide Gloss Model 683 by BYK Gardner (Catalogue #SP6831; 1997 version 3.26 D65/10°)

[0100] *Preparation of staining solution* (tea solution):

- 2 Lipton® tea bags were soaked in 500-mL of hot water for 1 day.
- Next day, the tea solution was filtered through FSI® 75 m filter bag, and pH of filtered tea solution (5.49) was measured.

[0101] *Preparation of Polymer Solutions:*

- Polymer solutions (3 or 10 w/w) were prepared by diluting the polymer with deionized water.

- Final pH of the polymer solution was adjusted with 18% NaOH solution to a target pH 6.5 (similar to pH environment in oral).
- The pH measurements and amount of neutralizer used are summarized in Table B1

[0102] *Preparation of Treated HAP Discs with Polymer Solutions:*

- Sintered or calcium deficient HAP discs were immersed in polymer solution (3 or 10% w/w at pH 6.5) for 1 minute.
- After the soak, the discs are rinsed with deionized water for 5 seconds to remove excess polymer solution and then dried with a paper towel.

[0103] *Staining Test:*

- HAP discs treated with polymer solution (3 or 10% w/w) and un-coated (as control) were immersed in tea solution and shaken for 24 hours at 200 rpm.
- At sampling time points (e.g., 1, 2, and 24 hour), the HAP discs were removed from the tea solution, and rinsed with D.I. water for ~ 30 seconds to clear any residual tea solution, dried with paper towel, and further dried in the air.
- The performance of the polymers is evaluated by visually comparing the color of polymer treated vs. untreated HAP discs.
- The stain test results are summarized in Table 6-9.

[0104] The stain test results are rated on a visual scale of 1 to 5, where 1 represents no stain (HAP discs before staining) and 5 represents intense staining (HAP discs without polymer treatment

and stained for 24h). A color reading was also measured on using the color meter, which measures a ΔE value. The lower the ΔE value the better.

Table 6. Stain test results for porous HAP discs treated with 3% polymer solution

Sample	Stain prevention @ 1h		Stain prevention @ 2h		Stain prevention @ 24h	
	Visual	ΔE	Visual	ΔE	Visual	ΔE
1	1	2.72	1	2.68	1.5	4.7
5	1	3.14	1	3.95	1.5	5.46
8	1	2.39	1	2.83	1	5.43
9	1	2.4	1.5	2.21	2	5.4
21	1	3.19	1	4.74	2	5.57
23	1	2.69	1	3.2	2	4.75
24	1	1.83	1.5	2.47	1.5	5.51
25	1	4.65	1	6.04	1.5	10.2
26	1	1.38	1	3.08	1.5	8.12
27	1	1.94	1.5	4.7	1.5	8.15
28	1	1.87	1	4.25	1.5	8.63
Comparative II	2	4.24	2.5	4.81	2.5	7.72
Carbopol® 907	2	4.01	3	4.85	4	12
Gantrez® S-97 BF	2	7.62	3	8.39	4	12
25% Slurry of Crest® Cavity Protection	2	20.5	3	23	4	25.8
25% Slurry of Crest® Tartar Protection	1.5	21.6	2	21.5	2	28
Control – untreated discs	3	23.5	4	26.6	5	32

Table 7 Stain test results for porous HAP discs treated with 10% polymer solution

Sample	Stain prevention @ 1h		Stain prevention @ 2h		Stain prevention @ 24h	
	Visual	ΔE	Visual	ΔE	Visual	ΔE
1	1	1.18	1	3.47	1.5	10.4
5	1	1.05	1	2.26	1.5	8.47
8	-	1.13	-	2.18	-	8.54
9	1	1.46	1.5	2.3	2	10.3
21	1	1.98	1.5	3.44	2	8.13

23	1	2.72	1.5	12.5	2	3.63
24	1	1.17	1	1.62	1	6.27
25	1	8.32	1	7.53	1	8.07
26	1	1.41	1	1.68	1.5	10.6
27	1	0.85	1	2.15	1.5	5.3
28	1	1.25	1	1.81	1.5	9.72
Comparative II	2	0.13	2.5	1.85	2.5	8.75
Carbopol® 907	2	8.43	2	11.7	3	13.5
Gantrez® S-97 BF	1.5	0.85	2	2.59	3	5.04
25% Slurry of Crest® Cavity Protection	2	20.5	3	23	4	25.8
25% Slurry of Crest® Tartar Protection	1.5	21.6	2	21.5	2	28
Control – untreated discs	3	23.5	4	26.6	5	32

Table 8. Stain test results for sintered HAP discs treated with 3% polymer solution

Sample	Stain prevention @ 1h	Stain prevention @ 2h	Stain prevention @ 24h
1	1.5	2	2
5	2.0	1.5	2
8	2	2	3
9	2	3	2
21	2	3	2.5
23	2	2	3
24	1.5	2	2
25	1.5	1.5	1.5
26	2	1.5	2.5
27	1	1.5	2
28	2	2.5	3
Comparative Example II	3	3	4
Carbopol® 907	1.5	2	3.5

Gantrez® S-97	2	2.5	3
BF			
25% Slurry of	2	2.5	3
Crest® Cavity			
Protection			
25% Slurry of	1.5	2	2
Crest® Tartar			
Protection			
Control – un-	2	3	5
treated discs			

Table 9. Stain test results for sintered HAP discs treated with 10% polymer solution

Sample	Stain prevention @ 1h	Stain prevention @ 2h	Stain prevention @ 24h
1	1	1	1.5
5	1	1	1.5
8	-	-	-
9	1.5	2.5	2
21	1.5	2.5	2.5
23	2	1.5	3
24	1	1	1
25	1	1	1
26	1.5	2	2.5
27	1.5	1	1.5
28	1.5	1.5	3
Comparative	1.5	2	4
Example II			
Carbopol® 907	1.5	2	3.5
Gantrez® S-97	2	2.5	3
BF			
25% Slurry of	2	2.5	3
Crest® Cavity			
Protection			
25% Slurry of	1.5	2	2

Crest® Tartar Protection			
Control – untreated discs	2	3	5

Table 10 Stain test results for porous HAP discs treated with 0.5% polymer solution

Sample	Stain prevention @ 1h	Stain prevention @ 2h
	ΔE	ΔE
1	16.28	19.3
5	14.22	15.81
8	15.66	18.86
9	NT	NT
21	NT	NT
23	14.72	18.79
24	15.3	16.64
25	13.38	15.45
26	NT	NT
27	NT	NT
28	NT	NT
Comparative II	14.9	17.64
Carbopol® 907	23.85	24.72
Gantrez® S-97 BF	21.71	22.11
25% Slurry of Crest® Cavity Protection	20.52	23.02
25% Slurry of Crest® Tartar Protection	21.59	21.52
Control - untreated discs	31.77	32.74

Table 11 Stain test results for porous
HAP discs treated with 1% polymer
solution

Sample	Stain prevention @ 1h	Stain prevention @ 2h
	ΔE	ΔE
1	8.83	12.66
5	7.24	9.28
8	6.89	9.45
9	NT	NT
21	NT	NT
23	9.39	10.06
24	8.02	9.31
25	8.9	10.06
26	NT	NT
27	NT	NT
28	NT	NT
Comparative II	NT	NT
Carbopol® 907	17.4	17.04
Gantrez® S- 97 BF	18.57	20.5
25% Slurry of Crest® Cavity Protection	20.52	23.02
25% Slurry of Crest® Tartar Protection	21.59	21.52
Control - untreated discs	31.77	32.74

[0105] Overall, the treated porous and sintered HAP discs with 0.5, 1, 3 or 10% (w/w) polymer solutions mentioned in this invention (including the comparative examples) showed better stain prevention performance than the control of this study (untreated porous and sintered HAP discs). Better stain prevention was observed for porous discs.

[0106] At all tested polymer concentrations and sampling points, both porous and sintered HAP discs coated with itaconic-containing polymers used as example polymers for this invention showed superior performance on stain prevention as compared to the discs coated with comparative polymers (Comparative Example II, Carbopol® 907, and Gantrez® S-97 BF). Better stain prevention was observed for porous discs.

[0107] The stain prevention performance of the treated porous and sintered HAP discs with 3% or 10% (w/w) itaconic-containing polymer solutions were compared with the discs treated with 25% slurry of commercial toothpastes (Crest® Cavity Protection and Crest® Tartar Protection). The treated porous HAP discs with polymer solutions exhibited greater stain prevention property than Crest® Cavity Protection toothpaste and slightly better performance than Crest® Tartar Protection toothpaste. The treated sintered discs gave slightly better or similar stain prevention performance than Commercial toothpastes.

[0108] Each of the documents referred to above is incorporated herein by reference, including any prior applications, whether or not specifically listed above, from which priority is claimed. The mention of any document is not an admission that such document qualifies as prior art or constitutes the general knowledge of the skilled person in any jurisdiction. Except in the Examples, or where otherwise explicitly indicated, all numerical quantities in this description specifying amounts of materials, reaction conditions, molecular weights,

number of carbon atoms, and the like, are to be understood as modified by the word "about." It is to be understood that the upper and lower amount, range, and ratio limits set forth herein may be independently combined. Similarly, the ranges and amounts for each element of the invention can be used together with ranges or amounts for any of the other elements. As used herein, the transitional term "comprising," which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, un-recited elements or method steps. However, in each recitation of "comprising" herein, it is also intended that the term encompass, as alternative embodiments, the phrases "consisting essentially of" and "consisting of," where "consisting of" excludes any element or step not specified and "consisting essentially of" permits the inclusion of additional un-recited elements or steps that do not materially affect the basic and novel characteristics of the composition or method under consideration.

What is claimed is:

1. An oral care composition comprising:
 - a) a safe and effective amount of an itaconic acid polymer or salts thereof, and
 - b) a pharmaceutically acceptable carrier.wherein said copolymer is substantially free of tri-substituted vinyl monomer impurities.
2. The oral care composition of claim 1, wherein the polymer of a) is a co-polymer comprising:
 - i. from about 10 mole percent to about 90 mole percent itaconic acid derived monomer groups, and
 - ii. from about 10 mole present to about 90 mole percent of at least one co-monomer:
3. The oral care composition of claim 2, wherein the co-monomer is derived from at least one of a C₁-C₁₈ alkyl (meth)acrylate, methyl acrylate, ethyl acrylate, butyl acrylate, 2-hydroxyethyl acrylate, 2-hydroxyethyl methacrylate, phosphate containing monomers, stearyl acrylate, polyethyleneglycol monomethylether acrylate, acrylamide, C₁-C₁₈ N-alkyl (meth)acrylamide, styrene substituted styrene, vinyl esters, acrylic acid, 2-acrylamido-2-methylpropane sulfonic acid, acrylamido methanesulfonic acid, maleic acid, polyunsaturated monomers and (meth)acrylonitrile.
4. The oral care composition of any previous claim, wherein said polymer is grafted with a polyol having a molecular weight of up to about 10000.
5. The oral care composition of any previous claim, wherein said copolymer comprises monomer units derived from itaconic acid at from about 30 to about 70 mole % and monomer units derived from acrylic acid at from about 30 to about 60 mole %.

6. The oral care composition of any of claims 1 to 4, wherein said polymer comprises monomer units derived from itaconic acid at from about 60 to about 70 mole %, monomer units derived from acrylic acid at from about 15 to about 20 mole % and monomer units derived from AMPS at from about 15 to about 20 mole %.
7. The oral care composition of any of claims 1 to 4, wherein said polymer comprises monomer units derived from itaconic acid and (meth)acrylic acid at from about 90 to about 99.9 mole % and monomer units derived from AMPS at from about 0.1 to about 10 mole %.
8. An oral care composition according to any previous claim wherein the number average molecular weight of the copolymer of a) is in the range of from about 500 to about 10,000,000.
9. An oral care composition according to any previous claim which comprises from about 0.01% to about 20.0% by weight of the copolymer of (a).
10. An oral care composition according to any previous claim which further comprises at least one acceptable oral care excipient.
11. The oral care composition according to any previous claim wherein the polymer is prepared in a reaction medium at a reaction temperature of between about 60 to about 85°C in the presence of from about 0.01 to about 5 mole percent polymerization initiator, based on the total amount of said monomer groups, and less than 5 equivalent% of a neutralizer per total itaconic acid monomer acid group.
12. The oral care composition of claim 11, wherein said itaconic acid monomer and from about 2 to about 25 % of said initiator

are dissolved in said medium and the remainder of said initiator is introduced over a period of about 2 to about 8 hours.

13. The oral care composition of either of claims 11 or 12 wherein said initiator is a redox system.
14. The oral care composition of claim 13, wherein said redox system comprises a sodium persulfate oxidizer and a reducer comprising a mixture of a disodium salt of 2-hydroxy-2-sulfinatoacetic acid and sodium sulfite.
15. The oral care composition of any of claims 11 to 14, where less than 20 mole % of the carboxylic acid functionality of the polymer has been neutralized.
16. The oral care composition of any previous claim wherein said polymer is present in a polymer solution comprising less than 2.5% w/w unreacted monomer based on the total weight of the polymer present in the solution.
17. The oral care composition of claim 16, wherein said polymer solution is characterized by a pH of greater than 1.8.
18. The oral care composition of claim 16 wherein said polymer solution is substantially transparent.
19. A method of preventing stains on hydroxyapatite comprising applying to the hydroxyapatite surface a safe and effective amount of an oral care composition according to any previous claim.

1/3

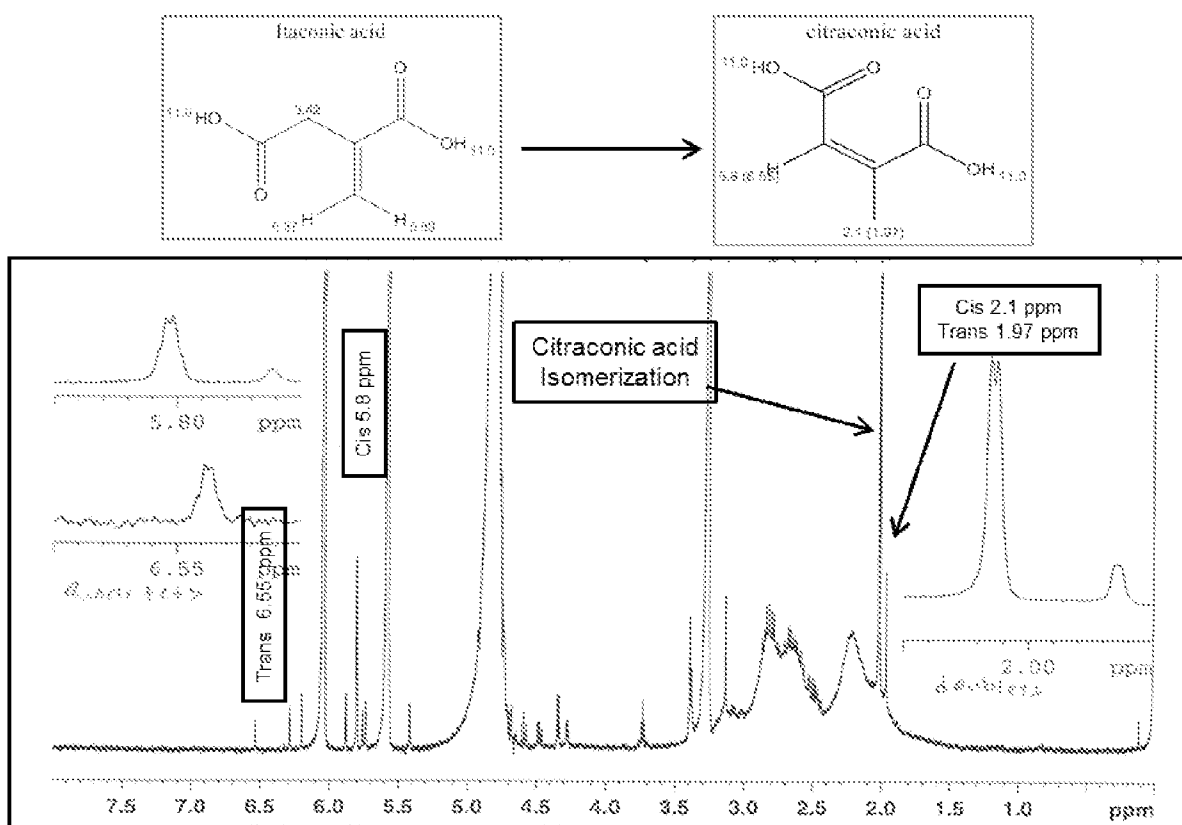


FIG. 1

FIGURE 2/3

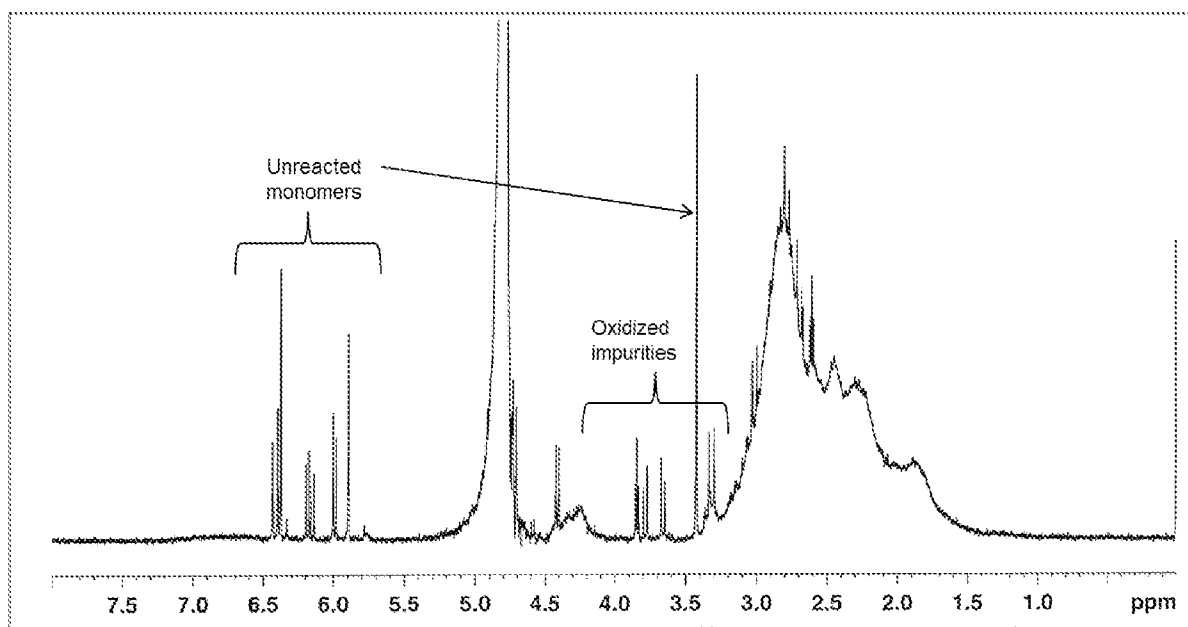


FIG. 2

3/3

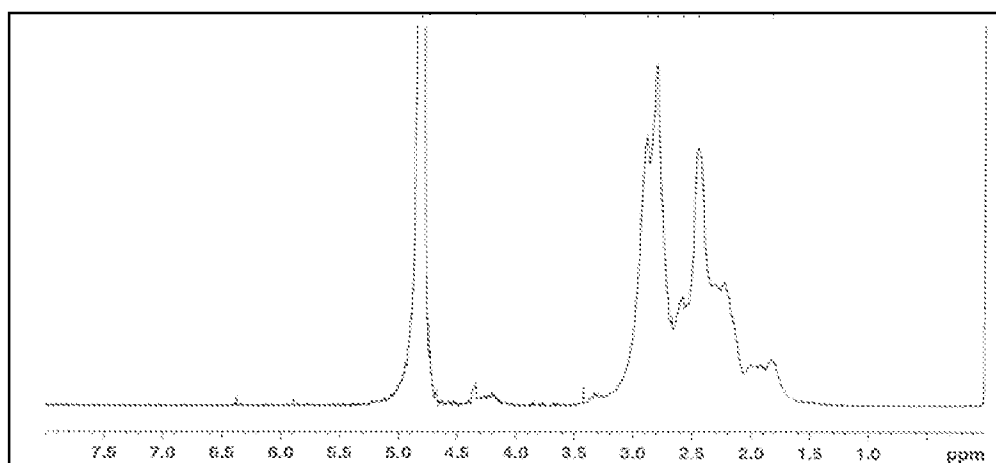


FIG. 3

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2014/025730

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61Q11/00 C08F220/06 C08F222/02
ADD.

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)
A61Q C08F

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 practicable, search terms used)

EP0-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 079 165 A2 (PFIZER [US]) 18 May 1983 (1983-05-18) page 3, line 8 - line 22; claim 1 -----	1-18
A	EP 0 506 246 A1 (ROHM & HAAS [US]) 30 September 1992 (1992-09-30) examples 3,8 -----	1-18
A	WO 2006/073822 A1 (COLGATE PALMOLIVE CO [US]; SHASTRY RAMACHANDRA [US]; MIRAJKAR YELLOJI) 13 July 2006 (2006-07-13) paragraph [0007]; claims 1,2 -----	1-18
A	US 4 138 477 A (GAFFAR MARIA CORAZON S) 6 February 1979 (1979-02-06) column 3, line 23 - line 31; example 2 ----- -/--	1-18

☒ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

27 August 2014

Date of mailing of the international search report

05/09/2014

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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2014/025730

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4 206 292 A (IIZUKA YO [JP] ET AL) 3 June 1980 (1980-06-03) claims 1-8 -----	1-18

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

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