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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
02 January 2025 (02.01.2025)

WIPO | PCT

(10) International Publication Number
WO 2025/002214 A1

(51) International Patent Classification:
A61K 8/19 (2006.01) *A61K 8/55* (2006.01)
A61K 8/24 (2006.01) *A61K 8/9789* (2017.01)
A61K 8/365 (2006.01) *A61Q 11/00* (2006.01)

(21) International Application Number:
PCT/CN2024/101836

(22) International Filing Date:
27 June 2024 (27.06.2024)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
PCT/CN2023/102976
28 June 2023 (28.06.2023) CN

(71) Applicant: **THE PROCTER & GAMBLE COMPANY** [US/US]; One Procter & Gamble Plaza, Cincinnati, Ohio 45202 (US).

(72) Inventors; and
(71) Applicants *(for US only)*: **ST. JOHN, Samuel James** [US/US]; One Procter & Gamble Plaza, Cincinnati, Ohio 45202 (US). **BAIG, Arif Ali** [US/US]; One Procter & Gamble Plaza, Cincinnati, Ohio 45202 (US). **STRAND, Ross** [GB/SG]; 70 Biopolis Street, Singapore 138547 (SG). **ZHU, Hanjiang** [CN/CN]; No. 35, Yu'an Road, B Zone, Tianzhu Konggang Development Zone, Shunyi District, Beijing 101312 (CN).

(74) Agent: **CHINA PATENT AGENT (H.K.) LTD.**; 22/F., Great Eagle Center, 23 Harbor Road, Wanchai, Hong Kong 999077 (CN).

(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, CV, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IQ, IR, IS, IT, JM, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, MG, MK, MN, MU, 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, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, CV, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SC, SD, SL, ST, 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, ME, 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))*

(54) **Title:** ORAL CARE COMPOSITIONS COMPRISING HOPS BETA ACIDS

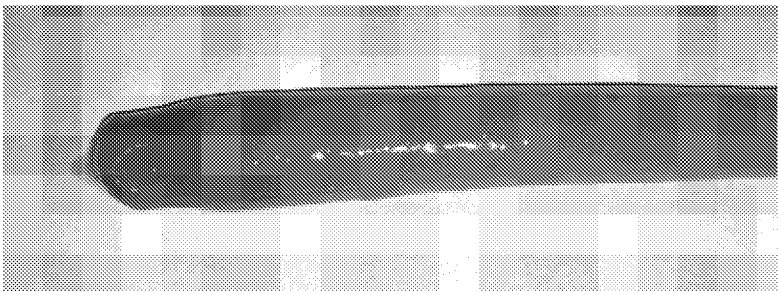


FIG. 1A

(57) **Abstract:** An oral care composition is provided and includes hops, residual iron, and a stabilization system comprising a polydentate polyphosphate having at least two functional groups, a polycarboxylate having at least three carboxylate groups, or a combination thereof.

WO 2025/002214 A1

ORAL CARE COMPOSITIONS COMPRISING HOPS BETA ACIDS

TECHNICAL FIELD

The disclosure relates generally present invention is directed to oral care compositions and, more particularly, relates to oral care compositions comprising hops with improved hops stability.

BACKGROUND

Oral care compositions, such as toothpaste and/or dentifrice compositions, can be applied to the oral cavity to clean and/or maintain the aesthetics and/or health of the teeth, gums, and/or tongue. Additionally, many oral care compositions are used to deliver active ingredients directly to oral care surfaces. Natural compounds with antibacterial activity, such as hops, can be incorporated into oral care compositions to provide antibacterial and/or anticavity activity. Natural antibacterial agents, such as hops, can include mixtures of active compounds, oils, flavonoids, and/or other flavor compounds. The use of hops beta acid extract in oral care compositions has the potential to delivered enhanced oral care benefits. Incorporating natural compounds into oral care compositions may affect the shelf-stability of the compositions. There is a need for oral care compositions with improved physical and chemical shelf-stability.

SUMMARY

An oral care composition is provided and includes hops acid, wherein the hops acid comprises hops alpha acid, hops beta acid, or a combination thereof, about 1 to about 1,000 μg per gram of the oral care composition of residual iron, and a stabilization system comprising a polydentate polyphosphate having at least two functional groups, a polycarboxylate having at least three carboxylate groups, or a combination thereof.

BRIEF DESCRIPTION OF THE DRAWINGS

The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

FIGS. 1A and 1B are photographs in color and grayscale, respectively, showing discoloration of example composition Ex. 1 following storage in a tube at 40 °C for one month.

FIGS. 2A and 2B are photographs in color and grayscale, respectively, showing the discoloration of various oral care compositions in a toothpaste tube following storage in a tube at room 20 °C for seven days.

FIGS. 3A and 3B are photographs in color and grayscale, respectively, showing the color of the centrifuged supernatant of various oral care compositions described in TABLE 4A.

FIG. 4 is a chart showing the color change of a toothpaste base due to the addition of hops.

DETAILED DESCRIPTION

Compositions comprising hops beta acid extract can experience color change over the product shelf life that make it unappealing for the consumer. Not wishing to be bound by theory, it is believed that the color change is related to the complexation of hops beta acids with ferric and ferrous ions in the composition that can further catalyze oxidation reactions in the presence of oxygen and browning reactions of those oxidative products. Importantly, there is a need to prevent the interaction of hops beta acids with ferrous and ferric ions in an oral care composition.

While not wishing to be bound by theory, it is believed that hops beta acids are susceptible to oxidative degradation yielding oxidation products, including 3-methyl-2-butental and 5,5-dimthyldimthyl-2(5H)-furanone. Since 5-dimthyl-2(5H)-furanone is further susceptible to a browning reaction, the oxidation of hops beta acids could sequentially impact the appearance stability of oral care compositions comprising hops beta acid extract. Another reaction pathway that can impact the color of oral care compositions comprising hops beta acid extract is complexation with ferrous or ferric ions. Iron is a known impurity from silica raw material. Iron can further be incorporated through abrasion of stainless-steel processing equipment in oral care compositions comprising silica or other dental abrasives. Hops beta acid complexes with ferrous or ferric ions have strong absorption in visible light region and can produce a brown to reddish to pinkish color in oral care compositions comprising both. This means the presence of iron impurity in oral care compositions comprising hops beta acid extract could risk color stability throughout the shelf life of the product potentially yielding a consumer unacceptable product.

Embodiments of the present invention are directed to oral care compositions comprising iron metal ion chelates to help reduce the interaction with hops beta acids with iron metal ions thus reducing the color change of the oral care composition or slowing the oxidative degradation of hops beta acids. Examples of the iron metal ion chelates include, for example, citrate-iron, bicarbonate-iron, carbonate-iron, EDTA-iron, polyphosphate-iron, such as pyrophosphate-iron, phytate-iron, and combinations thereof. The formation of these iron metal ion chelates can lead to reduce color change of oral care compositions comprising hops beta acid extract. In some embodiments, the stabilization system may include polydentate polyphosphate ($n > 2$) or polycarboxylate ($n > 3$) to prevent the discoloration of a hops beta acid extract in the presence of residual soluble iron.

The chelate effect postulates that complexes of polydentate ligands with a metal are more stable than the dentate-normalized equivalent of the monodentate-ligand-stabilized metal complex

(e.g., 1 mole of a bidentate ligand in comparison to 2 moles of a similarly structured monodentate ligand) because of a reduction in molar entropy of the bidentate chelate with respect to the monodentate complex. This can lead to an association and complex formation for polyvalent iron metal ions in the presence of iron metal ion chelates.

The complex can form spontaneously in solution in the presence of both iron metal ion and hops beta acid. Once formed, the iron metal ion can be stabilized in the composition, which can help to modulate its reactivity with formula components. While not wishing to being bound by theory, it is believed that the combination of iron metal ions and iron metal ion chelates can lead to an increase in color stability and hops beta acid stability in an oral care composition comprising both. The increase in color stability can be apparent in an aqueous composition.

In some embodiments, the stabilization system may include a chelant with an affinity for iron ions in either the ferrous (II) or ferric (III) forms. The affinity constant is conveniently expressed as the logarithm (log K1) and the larger the magnitude of this number, the stronger the association between the metal (iron ions in this case) and ligand. The strength of the association between a ligand and metal, in this case iron, can be termed iron affinity. A high iron binding affinity is required for chelators to effectively compete with iron salt impurities that reduce the stability compatibility. Affinity between a metal (M) and ligand (L) can be measured by the stepwise association constant, K1, which describes the following equilibrium:

$$M + L \leftrightharpoons ML;\ K_1 = \frac{[ML]}{[M][L]}$$

In some embodiments, the iron (III) metal ion chelate may have a log K1 greater than about 10, greater than about 13, greater than about 16, greater than about 18, or greater than about 20. In some embodiments, the iron (II) metal ion chelate may have a log K1 greater than about 2, greater than about 4, greater than about 5, greater than about 6, or greater than about 7.

Definitions

To define more clearly the terms used herein, the following definitions are provided. Unless otherwise indicated, the following definitions are applicable to this disclosure. If a term is used in this disclosure but is not specifically defined herein, the definition from the IUPAC Compendium of Chemical Terminology, 2nd Ed (1997), can be applied, as long as that definition does not conflict with any other disclosure or definition applied herein, or render indefinite or non-enabled any claim to which that definition is applied.

The term "oral care composition", as used herein, includes a product, which in the ordinary course of usage, is not intentionally swallowed for purposes of systemic administration of

particular therapeutic agents, but is rather retained in the oral cavity for a time sufficient to contact dental surfaces or oral tissues. Examples of oral care compositions include dentifrice, toothpaste, tooth gel, subgingival gel, emulsion, mouth rinse, mousse, foam, mouth spray, lozenge, chewable tablet, chewing gum, tooth whitening strips, floss and floss coatings, breath freshening dissolvable strips, unit-dose composition, fibrous composition, or denture care or adhesive product. The oral care composition may also be incorporated onto strips or films for direct application or attachment to oral surfaces, such as tooth whitening strips. Examples of emulsion compositions include the emulsions compositions of U.S. Patent No. 11,147,753, jammed emulsions, such as the jammed oil-in-water emulsions of U.S. Patent No. 11,096,874. Examples of unit-dose compositions include the unit-dose compositions of U.S. Patent Application Publication No. 2019/0343732.

The term "dentifrice composition", as used herein, includes tooth or subgingival -paste, gel, or liquid formulations unless otherwise specified. The dentifrice composition may be a single-phase composition or may be a combination of two or more separate dentifrice compositions. The dentifrice composition may be in any desired form, such as deep striped, surface striped, multilayered, having a gel surrounding a paste, or any combination thereof. Each dentifrice composition in a dentifrice comprising two or more separate dentifrice compositions may be contained in a physically separated compartment of a dispenser and dispensed side-by-side.

"Active and other ingredients" useful herein may be categorized or described herein by their cosmetic and/or therapeutic benefit or their postulated mode of action or function. However, it is to be understood that the active and other ingredients useful herein can, in some instances, provide more than one cosmetic and/or therapeutic benefit or function or operate *via* more than one mode of action. Therefore, classifications herein are made for the sake of convenience and are not intended to limit an ingredient to the particularly stated function(s) or activities listed.

The term "orally acceptable carrier" comprises one or more compatible solid or liquid excipients or diluents which are suitable for topical oral administration. By "compatible," as used herein, is meant that the components of the composition are capable of being commingled without interaction in a manner which would substantially reduce the composition's stability and/or efficacy. The carriers or excipients useful in embodiments of the present invention can include the usual and conventional components of mouthwashes or mouth rinses. Mouthwash or mouth rinse carrier materials typically include, but are not limited to one or more of water, alcohol, humectants, surfactants, and acceptance improving agents, such as flavoring, sweetening, coloring and/or cooling agents.

The term "substantially free" as used herein refers to the presence of no more than 0.05%, preferably no more than 0.01%, and more preferably no more than 0.001%, of an indicated material in a composition, by total weight of such composition.

The term "essentially free" as used herein means that the indicated material is not deliberately added to the composition, or preferably not present at analytically detectable levels. It is meant to include compositions whereby the indicated material is present only as an impurity of one of the other materials deliberately added.

The term "oral hygiene regimen" or "regimen" can be for the use of two or more separate and distinct treatment steps for oral health, e.g., toothpaste, mouth rinse, floss, toothpicks, spray, water irrigator, massager.

The term "total water content" as used herein means both free water and water that is bound by other ingredients in the oral care composition.

For the purpose of this description, the relevant molecular weight (MW) to be used is that of the material added when preparing the composition, e.g., if the chelant is a citrate species, which can be supplied as citric acid, sodium citrate or indeed other salt forms, the MW used is that of the particular salt or acid added to the composition but ignoring any water of crystallization that may be present.

While compositions and methods are described herein in terms of "comprising" various components or steps, the compositions and methods can also "consist essentially of" or "consist of" the various components or steps, unless stated otherwise.

As used herein, the word "or" when used as a connector of two or more elements is meant to include the elements individually and in combination; for example, X or Y, means X or Y or both.

As used herein, the articles "a" and "an" are understood to mean one or more of the material that is claimed or described, for example, "an oral care composition" or "a bleaching agent."

All measurements referred to herein are made at about 23 °C (i.e., room temperature) unless otherwise specified.

Generally, groups of elements are indicated using the numbering scheme indicated in the version of the periodic table of elements published in *Chemical and Engineering News*, 63(5), 27, 1985. In some instances, a group of elements can be indicated using a common name assigned to the group; for example, alkali metals for Group 1 elements, alkaline earth metals for Group 2 elements, and so forth.

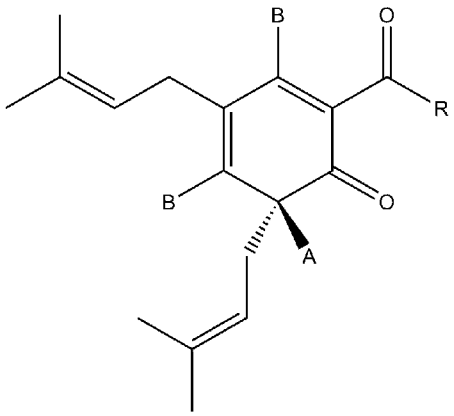
Several types of ranges are disclosed in relation to embodiments of the present invention. When a range of any type is disclosed or claimed, the intent is to disclose or claim individually each possible number that such a range could reasonably encompass, including end points of the range as well as any sub-ranges and combinations of sub-ranges encompassed therein.

The oral care composition can be in any suitable form, such as a solid, liquid, powder, paste, or combinations thereof. The oral care composition can be dentifrice, tooth gel, subgingival gel, mouth rinse, mousse, foam, mouth spray, lozenge, chewable tablet, chewing gum, tooth whitening strips, floss and floss coatings, breath freshening dissolvable strips, or denture care or adhesive product. The components of the dentifrice composition can be incorporated into a film, a strip, a foam, or a fiber-based dentifrice composition.

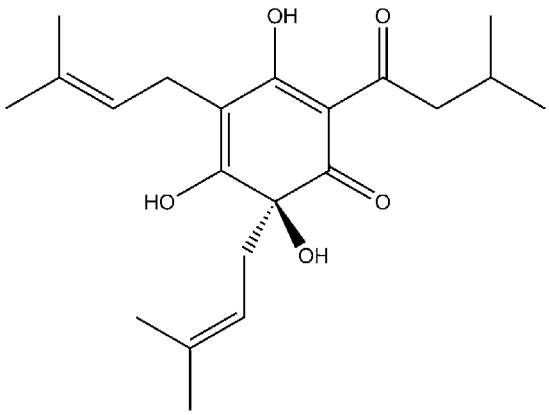
The oral care composition can include a variety of active and inactive ingredients, such as, for example, but not limited to a hops extract, a dicarboxylic acid, a tin ion source, a calcium ion source, water, a fluoride ion source, zinc ion source, one or more polyphosphates, humectants, surfactants, other ingredients, and the like, as well as any combination thereof, as described below. The section headers below are provided for organization and convenience only. In some cases, a compound can fall within one or more sections. For example, stannous fluoride can be a tin compound and/or a fluoride compound. Additionally, oxalic acid, or salts thereof, can be a dicarboxylic acid, a polydentate ligand, and/or a whitening agent.

Humulus lupulus

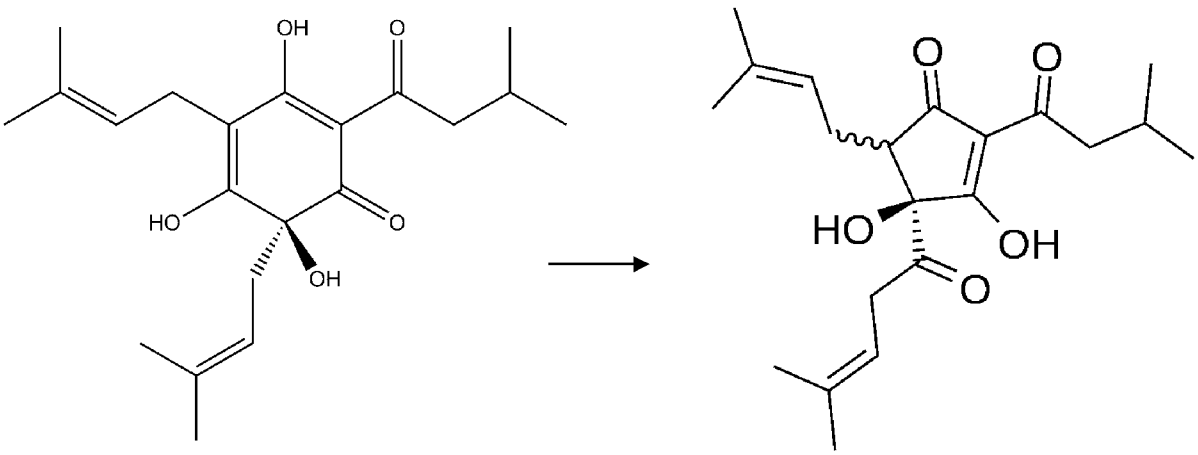
Oral care compositions of the present invention can comprise hops. The hops can comprise at least one hops compound from Formula I and/or Formula IV. The compound from Formula I and/or Formula IV can be provided by any suitable source, such as an extract from *Humulus lupulus* or Hops, *Humulus lupulus* itself, a synthetically derived compound, and/or salts, prodrugs, or other analogs thereof. The hops extract can comprise one or more hops alpha acids, one or more hops iso-alpha acids, one or more hops beta acids, one or more hops oils, one or more flavonoids, one or more solvents, and/or water. Suitable hops alpha acids (generically shown in Formula I) can include humulone (Formula II), adhumulone, cohumulone, posthumulone, prehumulone, and/or mixtures thereof. Suitable hops iso-alpha acids can include *cis*-isohumulone and/or *trans*-isohumulone. The isomerization of humulone into *trans*-isohumulone can be represented by Formula III.



Formula I. Hops Alpha Acids. A is the acidic hydroxyl functional group in the alpha position, B are the acidic hydroxyl functional groups in the beta position, and R is an alkyl functional group.

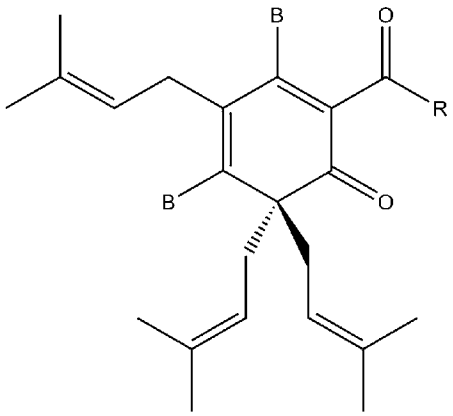


Formula II. Humulone

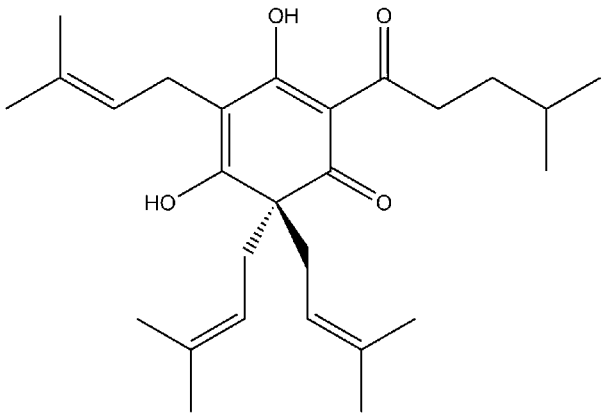


Formula III. Isomerization of Humulone to isohumulone.

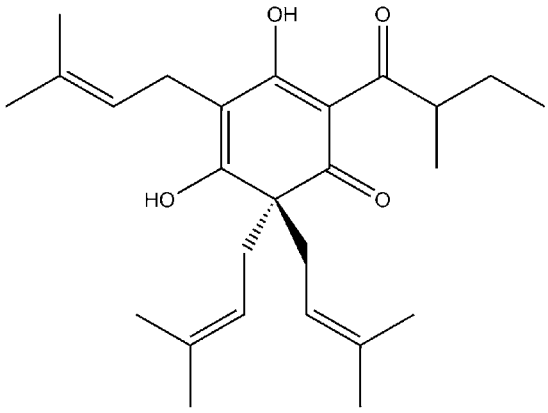
Suitable hops beta acids can include lupulone, adlupulone, colupulone, and/or mixtures thereof. A suitable hops beta acid can include a compound a described in Formula IV, V, VI, and/or VII.



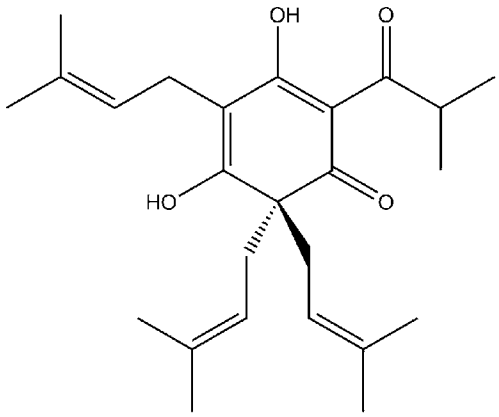
Formula IV. Hops Beta Acids. B are the acidic hydroxyl functional groups in the beta position and R is an alkyl functional group.



Formula V. Lupulone



Formula VI. Adlupulone



Formula VII. Colupulone

While hops alpha acids can demonstrate some antibacterial activity, hops alpha acids also have a bitter taste. The bitterness provided by hops alpha acids can be suitable for beer, but they are not suitable for use in oral care compositions. In contrast, hops beta acids can be associated with a higher antibacterial and/or anticaries activity, but not as bitter a taste. Thus, a hops extract with a higher proportion of beta acids to alpha acids than normally found in nature, can be suitable for use in oral care compositions for use as an antibacterial and/or anticaries agent.

A natural hops source can comprise from about 2% to about 12%, by weight of the hops source, of hops beta acids depending on the variety of hops. Hops extracts used in other contexts, such as in the brewing of beer, can comprise from about 15% to about 35%, by weight of the extract, of hops beta acids. The hops extract desired herein can comprise at least about 35%, at least about 40%, at least about 45%, from about 35% to about 95%, from about 40% to about 90%, or from about 45% to about 99%, of hops beta acids. The hops beta acids can be in an acidic form (i.e., with attached hydrogen atom(s) to the hydroxyl functional group(s)) or as a salt form.

A suitable hops extract is described in detail in U.S. Patent No. 7,910,140, which is herein incorporated by reference in its entirety. The hops beta acids and/or the hops alpha acids desired can be non-hydrogenated, partially hydrogenated by a non-naturally occurring chemical reaction, or hydrogenated by a non-naturally occurring chemical reaction. The hops beta acid can be essentially free of or substantially free of hydrogenated hops beta acid, hydrogenated hops alpha acid, and/or hydrogenated hops acid. A non-naturally occurring chemical reaction is a chemical reaction that was conducted with the aid of chemical compound not found within *Humulus lupulus*, such as a chemical hydrogenation reaction conducted with high heat not normally experienced by *Humulus lupulus* in the wild and/or a metal catalyst.

A natural hops source can comprise from about 2% to about 12%, by weight of the hops source, of hops alpha acids. Hops extracts used in other contexts, such as in the brewing of beer,

can comprise from about 15% to about 35%, by weight of the extract, of hops alpha acids. The hops extract desired herein can comprise less than about 10%, less than about 5%, less than about 1%, or less than about 0.5%, by weight of the extract, of hops alpha acids.

Hops oils can include terpene hydrocarbons, such as myrcene, humulene, caryophyllene, and/or mixtures thereof. The hops extract desired herein can comprise less than 5%, less than 2.5%, or less than 2%, by weight of the extract, of one or more hops oils.

Flavonoids present in the hops extract can include xanthohumol, 8-prenylnaringenin, isoxanthohumol, and/or mixtures thereof. The hops extract can be substantially free of, essentially free of, free of, or have less than 250 ppm, less than 150 ppm, and/or less than 100 ppm of one or more flavonoids.

As described in U.S. Patent No. 5,370,863, hops acids have been previously added to oral care compositions. However, the oral care compositions taught by U.S. Patent No. 5,370,863 only included up to 0.01%, by weight of the oral care composition. While not wishing to be bound by theory, it is believed that U.S. Patent No. 5,370,863 could only incorporate a low amount of hops acids because of the bitterness of hops alpha acids. A hops extract with a low level of hops alpha acids would not have this concern.

The hops compound can be combined with or free from an extract from another plant, such as a species from genus *Magnolia*. The hops compounds can be combined with or free from triclosan.

The hops compound can be combined with or free from an extract from another plant, such as a species from genus *Magnolia*, *Garcinia mangostana L.*, or *Zizyphus joazeiro*. The oral care composition may comprise less than about 0.5%, less than about 0.1%, or less than about 0.01% of an extract from a plant other than hops, such as a species from genus *Magnolia*, *Garcinia mangostana L.*, or *Zizyphus joazeiro*. The hops compounds can be combined with or free from a nonionic halogenated diphenyl ether, such as triclosan.

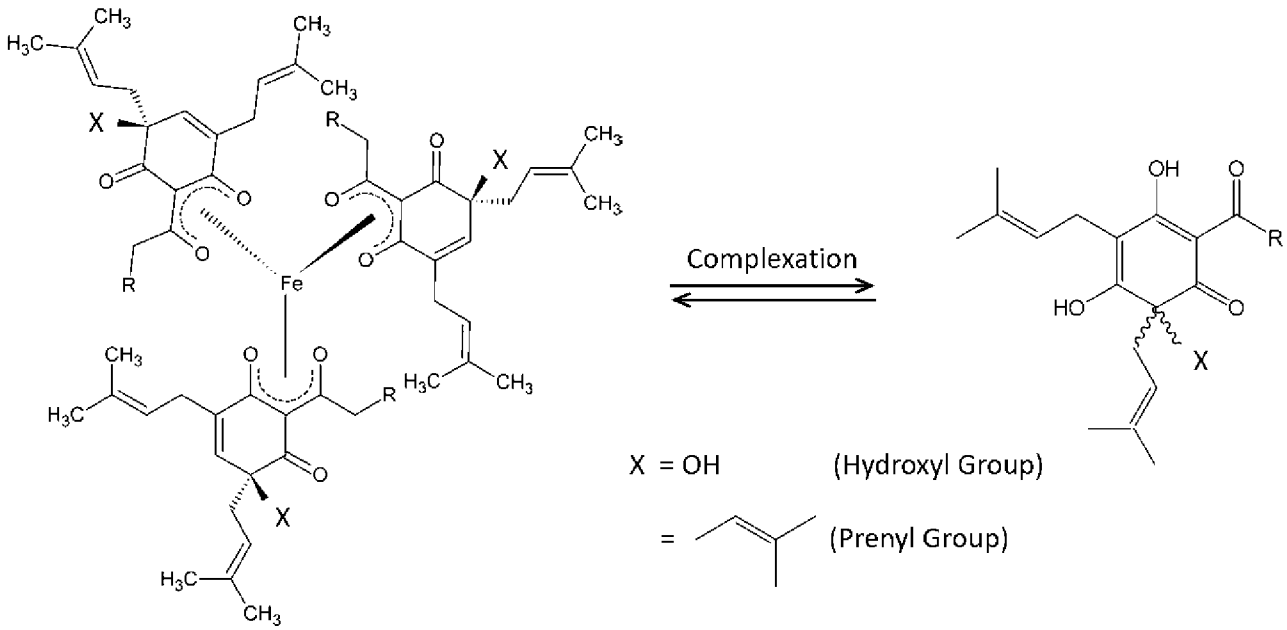
The oral care composition can comprise from about 0.01% to about 10%, greater than 0.01% to about 10%, from about 0.05%, to about 10%, from about 0.1% to about 10%, from about 0.2% to about 10%, from about 0.2% to about 10%, from about 0.2% to about 5%, from about 0.25% to about 2%, from about 0.05% to about 2%, or from greater than 0.25% to about 2%, of hops, such as hops beta acid, as described herein. The hops, such as the hops beta acid, can be provided by a suitable hops extract, the hops plant itself, or a synthetically derived compound. The hops, such as hops beta acid, can be provided as neutral, acidic compounds, and/or as salts with a suitable counter ion, such as sodium, potassium, ammonia, or any other suitable counter ion.

The hops can be provided by a hops extract, such as an extract from *Humulus lupulus* with at least 35%, by weight of the extract, of hops beta acid and less than 1%, by weight of the hops extract, of hops alpha acid. The oral care composition can comprise 0.01% to about 10%, greater than 0.01% to about 10%, from about 0.05%, to about 10%, from about 0.1% to about 10%, from about 0.2% to about 10%, from about 0.2% to about 10%, from about 0.2% to about 5%, from about 0.25% to about 2%, from about 0.05% to about 2%, or from greater than 0.25% to about 2%, of hops extract, as described herein.

Iron Complexation

In various embodiments, the composition may include residual iron in a range of from about 1 to about 1,000 μg/g, from about 10 μg/g to about 500 μg/g, or from about 10 μg/g to about 200 μg/g. Residual iron refers to iron that is present in the composition but is not deliberately added to the composition. It is meant to include compositions whereby the iron is present only as an impurity of one of the other materials deliberately added (e.g., silica) or that entered the composition during the manufacturing process.

Without wishing to be bound by theory, the following formula represents the complex formed from either hops alpha acid and iron (Formula VIII where X = OH) or hops beta acid and iron (Formula VIII where X = Prenyl Group).



Formula VIII. Hops Acid-Fe^{3+} Complex and Uncomplexed Hops Acid

Because the functional groups that interact with the iron are preserved between the alpha

and beta acids, a dark complex can form with either. Complexation of that residual iron with a chelant before it can interact with the hops acid improves both the appearance of the oral care composition and the chemical stability of the hops acids themselves.

The oral care composition can comprise from about 0.01% to about 15%, from about 0.1% to about 10%, from about 0.5% to about 5%, from about 1 to about 20%, or about 10% or less, by weight of the oral care composition, of a stabilization system comprising an iron metal ion chelate.

The iron metal ion chelate may comprise a polydentate polyphosphate having at least two functional groups, a polycarboxylate having at least three carboxylate groups, or a combination thereof. The iron metal ion chelate may have an affinity for ferrous (II) or ferric (III) iron ions, preferably wherein the iron metal ion chelate is an iron (II) metal ion chelate having a log K1 greater than about 2 or is an iron (III) metal ion chelate having a log K1 greater than about 10. Suitable polydentate polyphosphates include pyrophosphate, tripolyphosphate, polyphosphate, hexametaphosphate, phytate, or a combination thereof. Suitable polycarboxylates include ethylenediaminetetraacetic acid (EDTA) or citrate, such as zinc citrate, or sodium citrate. The stabilization system may include gluconate.

A change in color may be determined based on a comparison of L*a*b* values. In L*a*b* color space, "L" represents darkness to lightness, with values ranging from 0 to 100; "a" represents greenness to redness with values of -128 to +127; and "b" represents blueness to yellowness also with values from -128 to +127. The presence of a stabilization system may reduce the color change that would otherwise occur in a hops and iron containing composition.

In some embodiments, the addition of a stabilization system as described herein to an oral care composition comprising hops and iron results in a change in L* (ΔL) compared to the composition without the stabilization system of from about -5 to about 25, about -3 to about 25, about -1 to about 25, about 0 to about 25, about 0 to about 20, or about 0 to about 15.

In some embodiments, the addition of a stabilization system as described herein to an oral care composition comprising hops and iron results in a change in a* (Δa) compared to the composition without the stabilization system of from about -5 to about 1, about -5 about 0, about -3 to about 0, or about -2 to about 0.

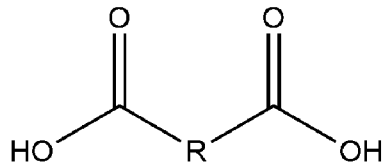
The addition of a stabilization system as described herein to an oral care composition comprising hops and iron results in a change in b* (Δb) compared to the composition without the stabilization system of, for example, from about -30 to about 1, about -25 about 0, about -25 to about -10, or about -20 to about 0.

The L* value can range from about 30, 40, or 50 to about 80, 90, or 100. The a* value can

range from -70, -50, -30 to 0 or from 0 to about 30, 50, or 70. The b* value can range from about -70, -50, -30 to 0 or from about 0 to about 15, 30, 50, or 70.

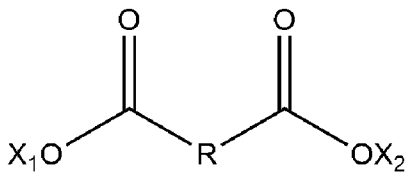
Dicarboxylic Acid

The oral care composition comprises dicarboxylic acid. The dicarboxylic acid comprises a compound with two carboxylic acid functional groups. The dicarboxylic acid can comprise a compound or salt thereof defined by Formula IX-A, Formula IX-B, and/or Formula IX-C.



Formula IX-A. Dicarboxylic acid

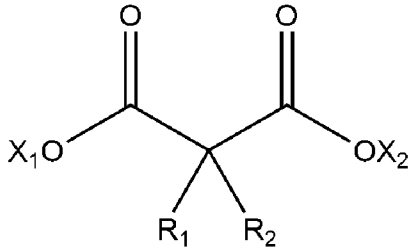
R can be null, alkyl, alkenyl, allyl, phenyl, benzyl, acetyl, aliphatic, aromatic, polyethylene glycol, polymer, O, N, P, or combinations thereof. R can also be additionally functionalized with one or more functional groups, such as -OH, $-NH_2$, and/or alkyl, alkenyl, aromatic, or combinations thereof.



Formula IX-B. Dicarboxylic acid

R can be null, alkyl, alkenyl, allyl, phenyl, benzyl, acetyl, aliphatic, aromatic, polyethylene glycol, polymer, O, N, P, or combinations thereof. R can also be additionally functionalized with one or more functional groups, such as -OH, $-NH_2$, and/or alkyl, alkenyl, aromatic, or combinations thereof.

X_1 and X_2 can independently be H, alkali metal, alkali earth metal, transition metal, or combinations thereof. Suitable alkali metals include lithium, sodium, potassium, or combinations thereof. Suitable alkali earth metals include magnesium, calcium, barium, or combinations thereof. Suitable transitional metals include titanium, chromium, iron, nickel, copper, zinc, tin, gold, silver, or combinations thereof.

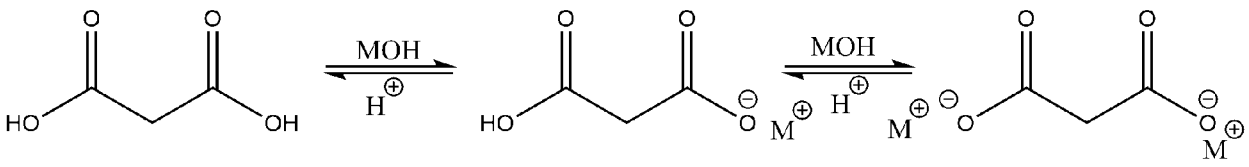


Formula IX-C. Dicarboxylic Acid.

R_1 can be null, alkyl, alkenyl, allyl, phenyl, benzyl, acetyl, aliphatic, aromatic, polyethylene glycol, polymer, O, N, P, or combinations thereof. R can also be additionally functionalized with one or more functional groups, such as -OH, -NH_2, and/or alkyl, alkenyl, aromatic, or combinations thereof.

X_1 and X_2 can independently be H, alkali metal, alkali earth metal, transition metal, or combinations thereof. Suitable alkali metals include lithium, sodium, potassium, or combinations thereof. Suitable alkali earth metals include magnesium, calcium, barium, or combinations thereof. Suitable transitional metals include titanium, chromium, iron, nickel, copper, zinc, tin, gold, silver, or combinations thereof.

The dicarboxylic acid can be added to a formulation as a neutral acid (as shown in Formula IX-A) or as a dicarboxylate monosalt (where one of the carboxylic acid functional groups is a salt and the other is neutral), a dicarboxylate disalt (where both of the carboxylic acid functional groups are salts), or combinations thereof. Additionally, as is well known to a person of ordinary skill in the art, whether or not that one or both of the carboxylic acid functional groups of the dicarboxylic acid are neutral or charged in solution, can be influenced by the pH of the solution. For example, a neutral dicarboxylic acid can be added to an aqueous solution and one or two protons from the two carboxylic acid functional groups can be removed if the pH is lower than the pKa of the carboxylic acid functional group, as shown below in Formula IX-D.



lower solution pH higher solution pH

Formula IX-D. Acid-Base Properties of Dicarboxylic Acid, wherein M is any metal.

The dicarboxylic acid can comprise oxalic acid, malonic acid, succinic acid, glutaric acid, adipic acid, pimelic acid, suberic acid, azerlaic acid, sebacic acid, undecanedioic acid, dodecanedioic acid, brassylic acid, thapsic acid, japanic acid, phellogenic acid, equisetolic acid, malic acid, maleic acid, tartaric acid, phthalic acid, methylmalonic acid, dimethylmalonic acid, tartronic acid, mesoxalic acid, dihydroxymalonic acid, dihydroxymalonic acid, fumaric acid, terephthalic acid, glutaric acid, salts thereof, or combinations thereof. The dicarboxylic acid can comprise suitable salts of dicarboxylic acid, such as, for example, when the dicarboxylic acid includes a salt of oxalic acid: monoalkali metal oxalate, dialkali metal oxalate, monopotassium monohydrogen oxalate, dipotassium oxalate, monosodium monohydrogen oxalate, disodium oxalate, titanium oxalate, and/or other metal salts of oxalate. The dicarboxylic acid can also include hydrates of the dicarboxylic acid and/or a hydrate of a salt of the dicarboxylic acid.

Suitable dicarboxylic acid compounds include malonic acid, methylmalonic acid, tartronic acid, malic acid, dimethylmalonic acid, mesoxalic acid, dihydroxymalonic acid, oxalic acid, salts thereof, or combinations thereof. These dicarboxylic acid compounds are particularly suitable as these compounds have been shown to have an unexpectedly high whitening benefit. While not wishing to be bound by theory, it is believed that particular dicarboxylic acid compounds have an unexpectedly high affinity to certain cationic crosslinking agents typically found in the colored matrix on the oral hard tissue surfaces, thereby resulting in the removal of stain from the surface.

Suitable dicarboxylic acid compounds include dicarboxylic acids described by Formula IX-A, wherein R is null, comprises a methylene or ethylene with one or two substitutions, and/or an acetyl group.

Without being bound by theory, it is hypothesized that the whitening efficacy of the dicarboxylics acids and their corresponding anions is driven by the ability of the dicarboxylic acid to reach and remove cationic bridges between chromophores and the tooth surface as well as chromophores and the pellicle proteins.

Fluoride

The oral care composition can comprise fluoride, which can be provided by a fluoride ion source. The fluoride ion source can comprise one or more fluoride containing compounds, such as stannous fluoride, sodium fluoride, titanium fluoride, calcium fluoride, calcium phosphate silicate fluoride, potassium fluoride, amine fluoride, sodium monofluorophosphate, zinc fluoride, and/or mixtures thereof.

The fluoride ion source and the tin ion source can be the same compound, such as for example, stannous fluoride, which can generate tin ions and fluoride ions. Additionally, the

fluoride ion source and the tin ion source can be separate compounds, such as when the tin ion source is stannous chloride and the fluoride ion source is sodium monofluorophosphate or sodium fluoride.

The fluoride ion source and the zinc ion source can be the same compound, such as for example, zinc fluoride, which can generate zinc ions and fluoride ions. Additionally, the fluoride ion source and the zinc ion source can be separate compounds, such as when the zinc ion source is zinc phosphate and the fluoride ion source is stannous fluoride.

The fluoride ion source can be essentially free of, or free of stannous fluoride. Thus, the oral care composition can comprise sodium fluoride, potassium fluoride, amine fluoride, sodium monofluorophosphate, zinc fluoride, and/or mixtures thereof.

The oral care composition can comprise a fluoride ion source capable of providing from about 50 ppm to about 5000 ppm, and preferably from about 500 ppm to about 3000 ppm of free fluoride ions. To deliver the desired amount of fluoride ions, the fluoride ion source may be present in the oral care composition at an amount of from about 0.0025% to about 5%, from about 0.01% to about 10%, from about 0.2% to about 1%, from about 0.5% to about 1.5%, or from about 0.3% to about 0.6%, by weight of the oral care composition. Alternatively, the oral care composition can comprise less than 0.1%, less than 0.01%, be essentially free of, be substantially free of, or be free of a fluoride ion source.

Metal

The oral care composition, as described herein, can comprise metal, which can be provided by a metal ion source comprising one or more metal ions. The metal ion source can comprise or be in addition to the tin ion source and/or the zinc ion source, as described herein. Suitable metal ion sources include compounds with metal ions, such as, but not limited to Sn, Zn, K, Cu, Mn, Mg, Sr, Ti, Fe, Mo, B, Ba, Ce, Al, In and/or mixtures thereof. The metal ion source can be any compound with a suitable metal and any accompanying ligands and/or anions.

Suitable ligands and/or anions that can be paired with metal ion sources include, but are not limited to acetate, ammonium sulfate, benzoate, bromide, borate, carbonate, chloride, citrate, gluconate, glycerophosphate, hydroxide, iodide, oxalate, oxide, propionate, D-lactate, DL-lactate, orthophosphate, pyrophosphate, sulfate, nitrate, tartrate, and/or mixtures thereof.

The oral care composition can comprise from about 0.01% to about 10%, from about 1% to about 5%, or from about 0.5% to about 15% of metal and/or a metal ion source.

Tin

An oral care composition according to embodiments of the present invention can comprise tin, which can be provided by a tin ion source. The tin ion source can be any suitable compound that can provide tin ions in an oral care composition and/or deliver tin ions to the oral cavity when the oral care composition is applied to the oral cavity. The tin ion source can comprise one or more tin containing compounds, such as stannous fluoride, stannous chloride, stannous bromide, stannous iodide, stannous oxide, stannous oxalate, stannous sulfate, stannous sulfide, stannic fluoride, stannic chloride, stannic bromide, stannic iodide, stannic sulfide, and/or mixtures thereof. Tin ion source can comprise stannous fluoride, stannous chloride, and/or mixture thereof. The tin ion source can also be a fluoride-free tin ion source, such as stannous chloride.

The oral care composition can comprise from about 0.0025% to about 5%, from about 0.01% to about 10%, from about 0.2% to about 1%, from about 0.4% to about 1%, or from about 0.3% to about 0.6%, by weight of the oral care composition, of tin and/or a tin ion source. Alternatively, the oral care composition can be essentially free of, substantially free of, or free of tin.

Antibacterial Agents

The oral care composition can comprise one or more antibacterial agents. Suitable antibacterial agents include any molecule that provides antibacterial activity in the oral cavity. Suitable antibacterial agents include hops acids, tin ion sources, benzyl alcohol, sodium benzoate, menthylglycyl acetate, menthyl lactate, L-menthol, o-neomenthol, chlorophyllin copper complex, phenol, oxyquinoline, and/or combinations thereof.

The oral care composition can comprise from about 0.01% to about 10%, from about 1% to about 5%, or from about 0.5% to about 15% of an antibacterial agent.

Bioactive Materials

The oral care composition can also include bioactive materials suitable for the remineralization of a tooth. Suitable bioactive materials include bioactive glasses, Novamin™, Recaldent™, hydroxyapatite, one or more amino acids, such as, for example, arginine, citrulline, glycine, lysine, or histidine, or combinations thereof. Suitable examples of compositions comprising arginine are found in U.S. Patent No. 4,154,813 and 5,762,911, which are herein incorporated by reference in their entirety. Other suitable bioactive materials include any calcium phosphate compound. Other suitable bioactive materials include compounds comprising a calcium source and a phosphate source.

Amino acids are organic compounds that contain an amine functional group, a carboxyl functional group, and a side chain specific to each amino acid. Suitable amino acids include, for example, amino acids with a positive or negative side chain, amino acids with an acidic or basic side chain, amino acids with polar uncharged side chains, amino acids with hydrophobic side chains, and/or combinations thereof. Suitable amino acids also include, for example, arginine, histidine, lysine, aspartic acid, glutamic acid, serine, threonine, asparagine, glutamine, cysteine, selenocysteine, glycine, proline, alanine, valine, isoleucine, leucine, methionine, phenylalanine, tyrosine, tryptophan, citrulline, ornithine, creatine, diaminobutonic acid, diaminoproprionic acid, salts thereof, and/or combinations thereof.

Bioactive glasses are comprising calcium and/or phosphate which can be present in a proportion that is similar to hydroxyapatite. These glasses can bond to the tissue and are biocompatible. Bioactive glasses can include a phosphopeptide, a calcium source, phosphate source, a silica source, a sodium source, and/or combinations thereof.

The oral care composition can comprise from about 0.01% to about 20%, from about 0.1% to about 10%, or from about 1% to about 10 % of a bioactive material by weight of the oral care composition.

Zinc

The oral care composition can comprise zinc, which can be provided by a zinc ion source. The zinc ion source can comprise one or more zinc containing compounds, such as zinc fluoride, zinc lactate, zinc oxide, zinc phosphate, zinc chloride, zinc acetate, zinc hexafluorozirconate, zinc sulfate, zinc tartrate, zinc gluconate, zinc citrate, zinc malate, zinc glycinate, zinc pyrophosphate, zinc metaphosphate, zinc oxalate, and/or zinc carbonate. The zinc ion source can be a fluoride-free zinc ion source, such as zinc phosphate, zinc oxide, and/or zinc citrate.

The zinc and/or zinc ion source may be present in the total oral care composition at an amount of from about 0.01% to about 10%, from about 0.2% to about 1%, from about 0.4% to about 1%, from about 0.5% to about 1.5%, or from about 0.3% to about 0.6%, by weight of the oral care composition. Alternatively, the oral care composition can be essentially free of, substantially free of, or free of zinc. In an embodiment, the oral care composition can be essentially free of, substantially free of, or free of soluble zinc.

Potassium

The oral care composition can comprise potassium, which can be provided by a potassium ion source. The potassium ion source can comprise one or more potassium containing compounds, such as potassium nitrate, potassium fluoride, potassium chloride, or combinations thereof.

The oral care composition can comprise from about 0.01% to about 10%, from about 0.2% to about 1%, from about 0.4% to about 1 %, or from about 0.3% to about 0.6%, by weight of the oral care composition, of potassium and/or potassium ion source. Alternatively, the oral care composition can be essentially free of, substantially free of, or free of potassium.

Quaternary Ammonium Compound

The oral care composition can include quaternary ammonium compound. The quaternary ammonium compounds in the compositions of embodiments of the present invention can include those in which one or two of the substitutes on the quaternary nitrogen has a carbon chain length (typically alkyl group) from about 8 to about 20, typically from about 10 to about 18 carbon atoms while the remaining substitutes (typically alkyl or benzyl group) have a lower number of carbon atoms, such as from about 1 to about 7 carbon atoms, typically methyl or ethyl groups. Cetylpyridinium chloride, cetyl pyridinium fluoride, tetradecylpyridinium chloride, N-tetradecyl-4-ethyl pyridinium chloride, domiphen bromide, benzalkonium chloride, benzethonium chloride, methyl benzethonium chloride, dodecyl trimethyl ammonium bromide, dodecyl dimethyl (2-phenoxyethyl) ammonium bromide, benzyl dimethoxystearyl ammonium chloride, quaternized 5-amino-1,3-bis(2-ethyl-hexyl)-5-methyl hexa hydropyrimidine, lauryl trimethylammonium chloride, cocoalkyl trimethylammonium chloride, cetyl trimethylammonium bromide, di-isobutylphenoxyethyl-dimethylbenzylammonium chloride, dodecyl trimethyl ammonium bromide, are exemplary of typical quaternary ammonium antimicrobial agents. Other compounds are bis[4-(R-amino)-1-pyridinium] alkanes as disclosed in U.S. No. 4,206,215 to Bailey. The pyridinium compounds are the preferred quaternary ammonium compounds, particularly preferred being cetylpyridinium, or tetradecylpyridinium halide salts (i.e., chloride, bromide, fluoride and iodide). Particularly preferred are cetylpyridinium chloride and fluoride salts.

The oral care composition can comprise at least about 0.025%, at least about 0.035%, at least about 0.045% to about 1.0%, from about 0.025% to about 1%, or from about 0.01% to about 10%, by weight of the composition, of the quaternary ammonium compound. Alternatively, the oral care composition can be essentially free of, substantially free of, or free of a quaternary ammonium compound.

pH

The pH of the oral care compositions as described herein can be from about 4 to about 10, from about 7 to about 10, greater than 7 to about 10, greater than 8 to about 10, greater than 7, greater than 7.5, greater than 8, greater than 9, from about 8.5 to about 10, from about 4 to about 7, from about 4 to about 6, from about 4.5 to about 6.5, from about 4.5 to about 5.5, from about 4 to less than 5.5, from about 4.5 to less than 5.5, greater than 4 to less than 5, greater than 4 to about 4.9, from about 4.9, from about 4 to about 5.4, from about 4 to about 5.3, from about 4 to about 5.2, from about 4 to about 5.1, from about 4 to about 5, from about 4 to about 4.9, from about 4 to about 4.8, from about 4 to about 4.7, or from about 4.8 to about 5.3, or from about 5.5 to about 9.5. The pH of a mouth rinse solution can be determined as the pH of the neat solution. The pH of a dentifrice composition can be determined as a slurry pH, which is the pH of a mixture of the dentifrice composition and water, such as a 1:4, 1:3, or 1:2 mixture of the dentifrice composition and water.

If the oral care composition comprises one or more dicarboxylic acids, a preferred pH is below about 7 or below about 6 due to the pKa of the dicarboxylic acid. While not wishing to be bound by theory, it is believed that the dicarboxylic acid displays unique behavior when the pH is below about 7 or below about 6, but surfaces in the oral cavity can also be sensitive to a low pH. Additionally, at pH values above about pH 7, the metal ion source can react with water and/or hydroxide ions to form insoluble metal oxides and/or metal hydroxides. The formation of these insoluble compounds can limit the ability of dicarboxylates to stabilize metal ions in oral care compositions and/or can limit the interaction of dicarboxylates with target metal ions in the oral cavity.

Additionally, at pH values less than 4, the potential for demineralization is greatly increased. Consequently, the oral care compositions comprising dicarboxylic acid, as described herein, can preferably have a pH from about 4 to about 7, from about 4 to about 6, from about 4.5 to about 6.5, from about 4 to about 5, from about 4 to less than 5, from about 4 to about 4.9, or from about 4.5 to less than 5.5 to minimize metal hydroxide/metal oxide formation and any increased demineralization in the oral cavity.

The pH of the oral care composition, as described herein, can be measured either immediately upon mixing, or upon aging the composition by placing the oral care composition at ambient or accelerated temperature and humidity conditions, such as including measuring the pH at a temperature of 25 °C, 30 °C and/or 40 °C with a 30%, 60% and/or 75% relative humidity for about 28 days or longer prior to measuring the pH.

Buffering Agents

The oral care composition can comprise one or more buffering agents. Buffering agents, as used herein, refer to agents that can be used to adjust the slurry pH of the oral care compositions. The buffering agents include alkali metal hydroxides, carbonates, sesquicarbonates, borates, silicates, phosphates, imidazole, carboxylates, and mixtures thereof. Specific buffering agents include monosodium phosphate, trisodium phosphate, sodium hydroxide, potassium hydroxide, alkali metal carbonate salts, sodium carbonate, imidazole, pyrophosphate salts, citric acid, and sodium citrate. The oral care composition can comprise one or more buffering agents each at a level of from about 0.1 % to about 30%, from about 1% to about 10%, or from about 1.5% to about 3%, by weight of the present composition.

Polyphosphate

The oral care composition can comprise polyphosphate, which can be provided by a polyphosphate source. A polyphosphate source can comprise one or more polyphosphate molecules. Polyphosphates are a class of materials obtained by the dehydration and condensation of orthophosphate to yield linear and cyclic polyphosphates of varying chain lengths. Thus, polyphosphate molecules are generally identified with an average number (n) of polyphosphate molecules, as described below. A polyphosphate is generally understood to consist of two or more phosphate molecules arranged primarily in a linear configuration, although some cyclic derivatives may be present.

Preferred polyphosphates are those having an average of two or more phosphate groups so that surface adsorption at effective concentrations produces sufficient non-bound phosphate functions, which enhance the anionic surface charge as well as hydrophilic character of the surfaces. Preferred polyphosphates include linear polyphosphates having the formula: $XO(XPO_3)_nX$, wherein X is sodium, potassium, ammonium, or any other alkali metal cations and n averages from about 2 to about 21. Alkali earth metal cations, such as calcium, are not preferred because they tend to form insoluble fluoride salts from aqueous solutions comprising a fluoride ions and alkali earth metal cations. Thus, the oral care compositions disclosed herein can be free of, essentially free of, or substantially free of calcium pyrophosphate.

Some examples of suitable polyphosphate molecules include, for example, pyrophosphate (n=2), tripolyphosphate (n=3), tetrapolyphosphate (n=4), sodaphos polyphosphate (n=6), hexaphos polyphosphate (n=13), benephos polyphosphate (n=14), hexametaphosphate (n=21), which is also known as Glass H. Polyphosphates can include those polyphosphate compounds manufactured by FMC Corporation, ICL Performance Products, and/or Astaris. Additional suitable polyphosphate

examples include a polydentate polyphosphate (n > 2) such as sodium acid pyrophosphate and sodium phytate.

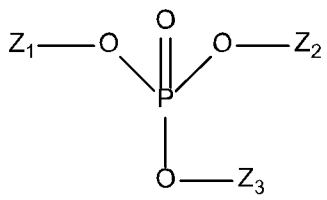
The oral care composition can comprise from about 0.01% to about 15%, from about 0.1% to about 10%, from about 0.5% to about 5%, from about 1 to about 20%, or about 10% or less, by weight of the oral care composition, of the polyphosphate source. Alternatively, the oral care composition can be essentially free of, substantially free of, or free of polyphosphate.

Surfactants

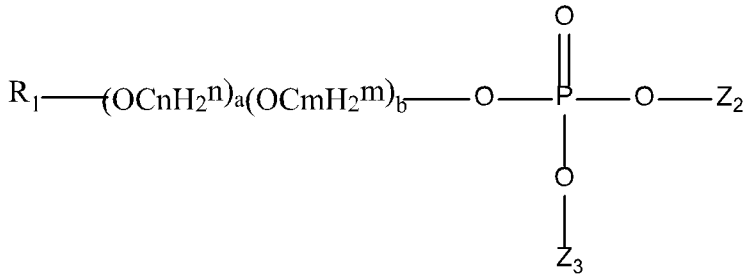
The oral care composition can comprise one or more surfactants. The surfactants can be used to make the compositions more cosmetically acceptable. The surfactant is preferably a detersive material which imparts to the composition detersive and foaming properties. Suitable surfactants are safe and effective amounts of anionic, cationic, nonionic, zwitterionic, amphoteric and betaine surfactants.

Suitable anionic surfactants include, for example, the water soluble salts of alkyl sulfates having from 8 to 20 carbon atoms in the alkyl radical and the water-soluble salts of sulfonated monoglycerides of fatty acids having from 8 to 20 carbon atoms. Sodium lauryl sulfate (SLS) and sodium coconut monoglyceride sulfonates are examples of anionic surfactants of this type. Other suitable anionic surfactants include sarcosinates, such as sodium lauroyl sarcosinate, taurates, sodium lauryl sulfoacetate, sodium lauroyl isethionate, sodium laureth carboxylate, and sodium dodecyl benzene sulfonate. Combinations of anionic surfactants can also be employed.

Another suitable class of anionic surfactants are alkyl phosphates. The surface active organophosphate agents can have a strong affinity for enamel surface and have sufficient surface binding propensity to desorb pellicle proteins and remain affixed to enamel surfaces. Suitable examples of organophosphate compounds include mono-, di- or triesters represented by the general structure below:



wherein Z_1, Z_2, or Z_3 may be identical or different with at least one being an organic moiety. Z_1, Z_2, or Z_3 can be selected from linear or branched, alkyl or alkenyl group of from 1 to 22 carbon atoms, optionally substituted by one or more phosphate groups; alkoxylated alkyl or alkenyl, (poly)saccharide, polyol or polyether group. Some other agents include alkyl or alkenyl phosphate esters represented by the following structure:

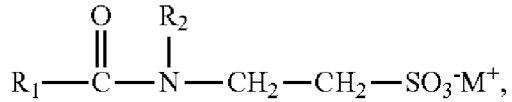


wherein R_1 represents a linear or branched, alkyl or alkenyl group of from 6 to 22 carbon atoms, optionally substituted by one or more phosphate groups; n and m, are individually and separately, 2 to 4, and a and b, individually and separately, are 0 to 20; Z and Z may be identical or different, each represents hydrogen, alkali metal, ammonium, protonated alkyl amine or protonated functional alkylamine, such as analkanolamine, or a R—(OCH2)(OCH) - group. Examples of suitable agents include alkyl and alkyl (poly)alkoxy phosphates such as lauryl phosphate; PPGS ceteareth-10 phosphate; laureth-1 phosphate; laureth-3 phosphate; laureth-9 phosphate; trilaureth-4 phosphate; C_{12-18} PEG 9 phosphate: and sodium dilaureth-10 phosphate. The alkyl phosphate can be polymeric. Examples of polymeric alkyl phosphates include those containing repeating alkoxy groups as the polymeric portion, in particular 3 or more ethoxy, propoxy isopropoxy or butoxy groups.

Other suitable anionic surfactants are sarcosinates, isethionates and taurates, especially their alkali metal or ammonium salts. Examples include: lauroyl sarcosinate, myristoyl sarcosinate, palmitoyl sarcosinate, stearoyl sarcosinate oleoyl sarcosinate, or combinations thereof.

Other suitable anionic surfactants include sodium or potassium alkyl sulfates, such as sodium lauryl sulfate, acyl isethionates, acyl methyl isethionates, alkyl ether carboxylates, acyl alaninates, acyl gulatames, acyl glycinates, acyl sarconsinates, sodium methyl acyl taurates, sodium laureth sulfosuccinates, alpha olefin sulfonates, alkyl benze sulfonates, sodium lauroyl lactylate, sodium laurylglucosides hydroxypropyl sulfonate, and/or combinations.

A suitable taurate surfactant is represented by the following formula:



wherein R_1 is a saturated or unsaturated, straight, or branched alkyl chain with 6 to 18 C atoms; R_2 is H or methyl, and M is H, sodium, or potassium. Preferably, the R_1 is a saturated or unsaturated, straight, or branched alkyl chain with 8 to 18 C atoms. Optionally but preferably, the taurate surfactant comprises one or more selected from the group consisting of potassium cocoyl taurate, potassium methyl cocoyl taurate, sodium caproyl methyl taurate, sodium cocoyl taurate, sodium

lauroyl taurate, sodium methyl cocoyl taurate, sodium methyl lauroyl taurate, sodium methyl myristoyl taurate, sodium methyl oleoyl taurate, and combinations thereof.

Zwitterionic or amphoteric surfactants useful herein include derivatives of aliphatic quaternary ammonium, phosphonium, and Sulfonium compounds, in which the aliphatic radicals can be straight chain or branched, and one of the aliphatic substituents contains from 8 to 18 carbon atoms and one contains an anionic water-solubilizing group, e.g., carboxy, sulfonate, sulfate, phosphate or phosphonate. Suitable betaine surfactants are disclosed in U.S. Pat. No. 5,180,577. Typical alkyl dimethyl betaines include decyl betaine or 2-(N-decyl-N,N-dimethylammonio) acetate, coco-betaine or 2-(N-coco-N,N-dimethyl ammonio)acetate, myristyl betaine, palmityl betaine, lauryl betaine, cetyl betaine, cetyl betaine, stearyl betaine, *etc.* The amidobetaines can be exemplified by cocoamidoethyl betaine, cocoamidopropyl betaine (CADB), and lauramidopropyl betaine. Other suitable amphoteric surfactants include betaines, sultaines, sodium laurylamphoacetates, alkylamphodiacetates, and/or combinations thereof.

Suitable cationic surfactants include, for example, derivatives of quaternary ammonium compounds having one long alkyl chain containing from 8 to 18 carbon atoms such as lauryl trimethylammonium chloride; cetyl pyridinium chloride; cetyl trimethyl-ammonium bromide; cetyl pyridinium fluoride or combinations thereof.

Suitable nonionic surfactants include, for example, compounds produced by the condensation of alkylene oxide groups (hydrophilic in nature) with an organic hydrophobic compound which may be aliphatic or alkylaromatic in nature. Examples of suitable nonionic surfactants can include the Pluronics® which are poloxamers, polyethylene oxide condensates of alkyl phenols, products derived from the condensation of ethylene oxide with the reaction product of propylene oxide and ethylene diamine, ethylene oxide condensates of aliphatic alcohols, long chain tertiary amine oxides, long chain tertiary phosphine oxides, long chain dialkyl sulfoxides and combinations of such materials. Other suitable non-ionic surfactants includes alkyl glucamides, alkyl glucosides, and/or combinations thereof.

The one or more surfactants can also include one or more natural and/or naturally derived surfactants. Natural surfactants can include surfactants that are derived from natural products and/or surfactants that are minimally or not processed. Natural surfactants can include hydrogenated, non-hydrogenated, or partially hydrogenated vegetable oils, olus oil, passiflora incarnata oil, candelilla cera, coco-caprylate, caprate, dicaprylyl ether, lauryl alcohol, myristyl myristate, dicaprylyl ether, caprylic acid, caprylic ester, octyl decanoate, octyl octanoate, undecane, tridecane, decyl oleate, oleic acid decylester, cetyl palmitate, stearic acid, palmitic acid,

glyceryl stearate, hydrogenated, non-hydrogenated, or partially hydrogenated vegetable glycerides, Polyglyceryl-2 dipolyhydroxystearate, cetearyl alcohol, sucrose polystearate, glycerin, octadodecanol, hydrolyzed, partially hydrolyzed, or non-hydrolyzed vegetable protein, hydrolyzed, partially hydrolyzed, or non-hydrolyzed wheat protein hydrolysate, polyglyceryl-3 diisostearate, glyceryl oleate, myristyl alcohol, cetyl alcohol, sodium cetearyl sulfate, cetearyl alcohol, glyceryl laurate, capric triglyceride, coco-glycerides, lectithin, dicaprylyl ether, xanthan gum, sodium coco-sulfate, ammonium lauryl sulfate, sodium cocoyl sulfate, sodium cocoyl glutamate, polyalkylglucosides, such as decyl glucoside, cetearyl glucoside, cetyl stearyl polyglucoside, coco-glucoside, and lauryl glucoside, and/or combinations thereof. Natural surfactants can include any of the NATRUE ingredients marketed by BASF, such as, for example, CegeSoft®, Cetiol®, Cutina®, Dehymuls®, Emulgade®, Emulgin®, Eutanol®, Gluadin®, Lameform®, LameSoft®, Lanette®, Monomuls®, Myritol®, Plantacare®, Plantaquat®, Platasil®, Rheocare®, Sulfopon®, Texapon®, and/or combinations thereof.

Other specific examples of surfactants include sodium lauryl sulfate, sodium lauryl isethionate, sodium lauroyl methyl isethionate, sodium cocoyl glutamate, sodium dodecyl benzene sulfonate, alkali metal or ammonium salts of lauroyl sarcosinate, myristoyl sarcosinate, palmitoyl sarcosinate, stearoyl sarcosinate and oleoyl sarcosinate, polyoxyethylene sorbitan monostearate, isostearate and laurate, sodium lauryl sulfoacetate, N-lauroyl sarcosine, the sodium, potassium, and ethanolamine salts of N-lauroyl, N-myristoyl, or N-palmitoyl sarcosine, polyethylene oxide condensates of alkyl phenols, cocoamidopropyl betaine, lauramidopropyl betaine, palmityl betaine, sodium cocoyl glutamate, and the like. Additional surfactants desired include fatty acid salts of glutamate, alkyl glucoside, salts of taurates, betaines, caprylates, and/or mixtures thereof. The oral care composition can also be sulfate free. The oral care composition can comprise one or more surfactants each at a level from about 0.01% to about 15%, from about 0.3% to about 10%, or from about 0.3% to about 2.5 %, by weight of the oral care composition.

Monodentate Ligand

The oral care composition can comprise monodentate ligand having a molecular weight (MW) of less than 1000 g/mol. A monodentate ligand has a single functional group that can interact with the central atom, such as a tin ion. The monodentate ligand must be suitable for the use in oral care composition, which can be include being listed in Generally Regarded as Safe (GRAS) list with the United States Food and Drug Administration or other suitable list in a jurisdiction of interest.

The monodentate ligand, as described herein, can include a single functional group that can chelate to, associate with, and/or bond to tin. Suitable functional groups that can chelate to, associate with, and/or bond to tin include carbonyl, amine, among other functional groups known to a person of ordinary skill in the art. Suitable carbonyl functional groups can include carboxylic acid, ester, amide, or ketones.

The monodentate ligand can comprise a single carboxylic acid functional group. Suitable monodentate ligands comprising carboxylic acid can include compounds with the formula R-COOH, wherein R is any organic structure. Suitable monodentate ligands comprising carboxylic acid can also include aliphatic carboxylic acid, aromatic carboxylic acid, sugar acid, salts thereof, and/or combinations thereof.

The aliphatic carboxylic acid can comprise a carboxylic acid functional group attached to a linear hydrocarbon chain, a branched hydrocarbon chain, and/or cyclic hydrocarbon molecule. The aliphatic carboxylic acid can be fully saturated or unsaturated and have one or more alkene and/or alkyne functional groups. Other functional groups can be present and bonded to the hydrocarbon chain, including halogenated variants of the hydrocarbon chain. The aliphatic carboxylic acid can also include hydroxyl acids, which are organic compounds with an alcohol functional group in the alpha, beta, or gamma position relative to the carboxylic acid functional group. A suitable alpha hydroxy acid includes lactic acid and/or a salt thereof.

The aromatic carboxylic acid can comprise a carboxylic acid functional group attached to at least one aromatic functional group. Suitable aromatic carboxylic acid groups can include benzoic acid, salicylic acid, and/or combinations thereof.

The carboxylic acid can include formic acid, acetic acid, propionic acid, butyric acid, valeric acid, caproic acid, enanthic acid, caprylic acid, ascorbic acid, benzoic acid, caprylic acid, cholic acid, glycine, alanine, valine, isoleucine, leucine, phenylalanine, linoleic acid, niacin, oleic acid, propanoic acid, sorbic acid, stearic acid, gluconate, lactate, carbonate, chloroacetic acid, dichloroacetic acid, trichloroacetic acid, salts thereof, and/or combinations thereof.

The oral care composition can include from about 0.01% to about 10%, from about 0.1% to about 15%, from about 1% to about 5%, or from about 0.0001 to about 25%, by weight of the composition, of the monodentate ligand.

Polydentate Ligand

The oral care composition can comprise polydentate ligand having a molecular weight (MW) of less than 1000 g/mol or less than 2500 g/mol. A polydentate ligand has at least two functional groups that can interact with the central atom, such as a tin ion. Additionally, the

polydentate ligand must be suitable for the use in oral care composition, which can be include being listed in Generally Regarded as Safe (GRAS) list with the United States Food and Drug Administration or another suitable list in a jurisdiction of interest.

The polydentate ligand, as described herein, can include at least two functional groups that can chelate to, associate with, and/or bond to tin. The polydentate ligand can comprise a bidentate ligand (i.e., with two functional groups), tridentate (i.e., with three functional groups), tetradentate (i.e., with four functional groups), etc.

Suitable functional groups that can chelate to, associate with, and/or bond to tin include carbonyl, phosphate, nitrate, amine, among other functional groups known to a person of ordinary skill in the art. Suitable carbonyl functional groups can include carboxylic acid, ester, amide, or ketones.

The polydentate ligand can comprise two or more carboxylic acid functional groups. Suitable polydentate ligands comprising carboxylic acid can include compounds with the formula HOOC-R-COOH, wherein R is any organic structure. Suitable polydentate ligands comprising two or more carboxylic acid can also include dicarboxylic acid, tricarboxylic acid, tetracarboxylic acid, *etc*.

Other suitable polydentate ligands include compounds comprising at least two phosphate functional groups. Thus, the polydentate ligand can comprise polyphosphate, as described herein.

Other suitable polydentate ligands include hops beta acids, such as lupulone, colupulone, adlupulone, and/or combinations thereof. The hops beta acid can be synthetically derived and/or extracted from a natural source.

The polydentate ligand can also include phosphate as the functional group to interact with the tin. Suitable phosphate compounds include phosphate salts, organophosphates, or combinations thereof. Suitable phosphate salts include salts of orthophosphate, hydrogen phosphate, dihydrogen phosphate, alkylated phosphates, and combinations thereof. The polydentate ligand can comprise oxalic acid, malonic acid, succinic acid, glutaric acid, adipic acid, pimelic acid, suberic acid, azerlaic acid, sebacic acid, undecanedioic acid, dodecanedioic acid, brassylic acid, thapsic acid, japanic acid, phellogenic acid, equisetolic acid, maleic acid, malic acid, tartaric acid, phthalic acid, citric acid, phytic acid, pyrophosphate, tripolyphosphate, tetrapolyphosphate, hexametaphosphate, salts thereof, and/or combinations thereof.

The oral care composition can include from about 0.01% to about 10%, from about 0.1% to about 15%, from about 1% to about 5%, or from about 0.0001 to about 25%, by weight of the composition, of the polydentate ligand.

Thickening Agent

The oral care composition can comprise one or more thickening agents. Thickening agents can be useful in the oral care compositions to provide a gelatinous structure that stabilizes the composition against phase separation. Suitable thickening agents include polysaccharides, polymers, and/or silica thickeners.

The thickening agent can comprise one or more polysaccharides. Some non-limiting examples of polysaccharides include starch; glycerite of starch; gums such as gum karaya (sterculia gum), gum tragacanth, gum arabic, gum ghatti, gum acacia, xanthan gum, guar gum and cellulose gum; magnesium aluminum silicate (Veegum); carrageenan; sodium alginate; agar-agar; pectin; gelatin; cellulose compounds such as cellulose, microcrystalline cellulose, carboxymethyl cellulose, hydroxyethyl cellulose, hydroxypropyl cellulose, hydroxymethyl cellulose, hydroxymethyl carboxypropyl cellulose, methyl cellulose, ethyl cellulose, and sulfated cellulose; natural and synthetic clays such as hectorite clays; and mixtures thereof.

Other polysaccharides that are suitable for use herein include carageenans, gellan gum, locust bean gum, xanthan gum, carbomers, poloxamers, modified cellulose, and mixtures thereof. Carageenan is a polysaccharide derived from seaweed. There are several types of carageenan that may be distinguished by their seaweed source and/or by their degree of and position of sulfation. The thickening agent can comprise kappa carageenans, modified kappa carageenans, iota carageenans, modified iota carageenans, lambda carrageenan, and mixtures thereof. Carageenans suitable for use herein include those commercially available from the FMC Company under the series designation "Viscarin," including but not limited to Viscarin TP 329, Viscarin TP 388, and Viscarin TP 389.

The thickening agent can comprise one or more polymers. The polymer can be a polyethylene glycol (PEG), a polyvinylpyrrolidone (PVP), polyacrylic acid, a polymer derived from at least one acrylic acid monomer, a copolymer of maleic anhydride and methyl vinyl ether, a crosslinked polyacrylic acid polymer, of various weight percentages of the oral care composition as well as various ranges of average molecular ranges. Alternatively, the oral care composition can be free of, essentially free of, or substantially free of a copolymer of maleic anhydride and methyl vinyl ether. The polymer can comprise polyacrylate crosspolymer, such as polyacrylate crosspolymer-6. Suitable sources of polyacrylate crosspolymer-6 can include Sepimax Zen™ commercially available from Seppic.

The thickening agent can comprise inorganic thickening agents. Some non-limiting examples of suitable inorganic thickening agents include colloidal magnesium aluminum silicate,

silica thickeners. Useful silica thickeners include, for example, include, as a non-limiting example, an amorphous precipitated silica such as ZEODENT® 165 silica. Other non-limiting silica thickeners include ZEODENT® 153, 163, and 167, and ZEOFREE® 177 and 265 silica products, all available from Evonik Corporation, and AEROSIL® fumed silicas.

The oral care composition can comprise from 0.01% to about 15%, from 0.1% to about 10%, from about 0.2% to about 5%, or from about 0.5 % to about 2% of one or more thickening agents.

Abrasive

The oral care composition of embodiments of the present invention can comprise an abrasive. Abrasives can be added to oral care formulations to help remove surface stains from teeth. The oral care can include a calcium abrasive and/or a non-calcium abrasive, such as a silica abrasive.

The oral care composition can comprise a calcium abrasive. The calcium abrasive can be any suitable abrasive compound that can provide calcium ions in an oral care composition and/or deliver calcium ions to the oral cavity when the oral care composition is applied to the oral cavity. The oral care composition can comprise from about 5% to about 70%, from about 10% to about 60%, from about 20% to about 50%, from about 25% to about 40%, or from about 1% to about 50% of a calcium abrasive. The calcium abrasive can comprise one or more calcium abrasive compounds, such as calcium carbonate, precipitated calcium carbonate (PCC), ground calcium carbonate (GCC), chalk, dicalcium phosphate, calcium pyrophosphate, and/or mixtures thereof.

The oral care composition can comprise a non-calcium abrasive such as bentonite, silica gel (by itself, and of any structure), precipitated silica, amorphous precipitated silica (by itself, and of any structure as well), hydrated silica, perlite, titanium dioxide, calcium pyrophosphate, dicalcium phosphate dihydrate, alumina, hydrated alumina, calcined alumina, aluminum silicate, insoluble sodium metaphosphate, insoluble potassium metaphosphate, insoluble magnesium carbonate, zirconium silicate, particulate thermosetting resins and other suitable abrasive materials. Such materials can be introduced into the oral care compositions to tailor the polishing characteristics of the target dentifrice formulation. The oral care composition can comprise from about 5% to about 70%, from about 10% to about 50%, from about 10% to about 60%, from about 20% to about 50%, from about 25% to about 40%, or from about 1% to about 50%, by weight of the oral care composition, of the non-calcium abrasive.

Alternatively, the oral care composition can be essentially free of, substantially free of, essentially free of, or free of silica, alumina, or any other non-calcium abrasive. The oral care

composition can comprise less than about 5%, less than about 1%, less than about 0.5%, less than about 0.1%, or 0% of a non-calcium abrasive, such as silica and/or alumina.

The oral care composition can also comprise a silica abrasive, such as silica gel (by itself, and of any structure), precipitated silica, amorphous precipitated silica (by itself, and of any structure as well), hydrated silica, and/or combinations thereof. The oral care composition can comprise from about 5% to about 70%, from about 10% to about 60%, from about 10% to about 50%, from about 20% to about 50%, from about 25% to about 40%, or from about 1% to about 50% of a silica abrasive.

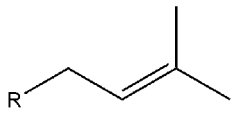
Where the oral care composition comprises a dicarboxylic acid, the oral care composition can include a low level of or no abrasive as the dicarboxylic acid can provide a high enough whitening benefit that an abrasive is not necessary.

While mouth rinse compositions typically do not include abrasive, dentifrice compositions typically do include abrasive. However, the dentifrice compositions and/or toothpaste compositions of embodiments of the present invention can include a low level of or no abrasive. As such, the oral care composition or dentifrice composition can comprise less than about 5%, from about 0.5% to about 2%, or less than about 2%, by weight of the composition, of abrasive. The oral care composition or dentifrice composition can also be essentially free of, substantially free of, or free of abrasive.

Prenylated Flavonoids

The oral care composition can comprise prenylated flavonoid. Flavonoids are a group of natural substances found in a wide range of fruits, vegetables, grains, bark, roots, stems, flowers, tea, and wine. Flavonoids can have a variety of beneficial effects on health, such as antioxidative, anti-inflammatory, antimutagenic, anticarcinogenic, and antibacterial benefits. Prenylated flavonoids are flavonoids that include at least one prenyl functional group (3-methylbut-2-en-1-yl, as shown in Formula X), which has been previously identified to facilitate attachment to cell membranes. Thus, while not wishing to being bound by theory, it is believed that the addition of a prenyl group, i.e., prenylation, to a flavonoid can increase the activity of the original flavonoid by increasing the lipophilicity of the parent molecule and improving the penetration of the prenylated molecule into the bacterial cell membrane. Increasing the lipophilicity to increase penetration into the cell membrane can be a double-edged sword because the prenylated flavonoid will tend towards insolubility at high Log P values (high lipophilicity). Log P can be an important indicator of antibacterial efficacy.

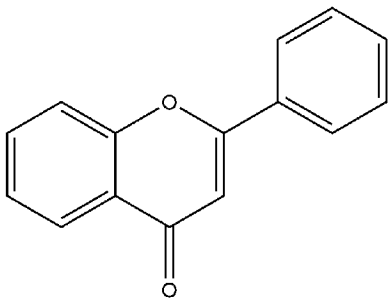
As such, the term prenylated flavonoids can include flavonoids found naturally with one or more prenyl functional groups, flavonoids with a synthetically added prenyl functional group, and/or prenylated flavonoids with additional prenyl functional groups synthetically added.



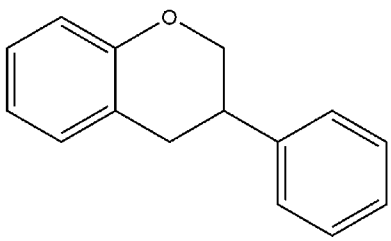
Formula X. Prenyl Function Group with R representing the other portions of the molecule

Other suitable functionalities of the parent molecule that improve the structure-activity relationship (e.g., structure-MIC relationship) of the prenylated molecule include additional heterocycles containing nitrogen or oxygen, alkylamino chains, or alkyl chains substituted onto one or more of the aromatic rings of the parent flavonoid.

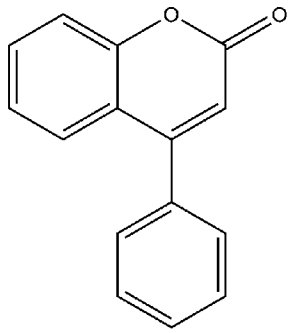
Flavonoids can have a 15-carbon skeleton with at least two phenyl rings and at least one heterocyclic ring. Some suitable flavonoid backbones can be shown in Formula XI (flavone backbone), Formula XII (isoflavan backbone), and/or Formula XIII (neoflavonoid backbone).



Formula XI. Flavone Backbone



Formula XII. Isoflavan Backbone



Formula XIII. Neoflavanoid Backbone

Other suitable subgroups of flavonoids include anthocyanidins, anthoxanthins, flavanones, flavanonols, flavans, isoflavonoids, chalcones and/or combinations thereof.

Prenylated flavonoids can include naturally isolated prenylated flavonoids or naturally isolated flavonoids that are synthetically altered to add one or more prenyl functional groups through a variety of synthetic processes that would be known to a person of ordinary skill in the art of synthetic organic chemistry.

Other suitable prenylated flavonoids can include Bavachalcone, Bavachin, Bavachinin, Corylifol A, Epimedin A, Epimedin A1, Epimedin B, Epimedin C, Icariin, Icariside I, Icariside II, Icaritin, Isobavachalcone, Isoxanthohumol, Neobavaisoflavone, 6-Prenylnaringenin, 8-Prenylnaringenin, Sophoraflavanone G, (-)-Sophoranone, Xanthohumol, Quercetin, Macelignan, Kuraridin, Kurarinone, Kuwanon G, Kuwanon C, Panduratin A, 6-geranylnaringenin, Australone A, 6,8-Diprenyleriodictyol, dorsmanin C, dorsmanin F, 8-Prenylkaempferol, 7-O-Methylluteone, luteone, 6-prenylgenistein, isowighteone, lupiwighteone, and/or combinations thereof. Other suitable prenylated flavonoids include cannflavins, such as Cannflavin A, Cannflavin B, and/or Cannflavin C.

Preferably, the prenylated flavonoid has a high probability of having a MIC of less than about 25 ppm for *S. aureus*, a gram-positive bacterium. Suitable prenylated flavonoids include Bavachin, Bavachinin, Corylifol A, Icaritin, Isoxanthohumol, Neobavaisoflavone, 6-Prenylnaringenin, 8-Prenylnaringenin, Sophoraflavanone G, (-)-Sophoranone, Kurarinone, Kuwanon C, Panduratin A, and/or combinations thereof.

Preferably, the prenylated flavonoid has a high probability of having a MIC of less than about 25 ppm for *E. coli*, a gram-negative bacterium. Suitable prenylated flavonoids include Bavachinin, Isoxanthohumol, 8-Prenylnaringenin, Sophoraflavanone G, Kurarinone, Panduratin A, and/or combinations thereof.

Approximately 1000 prenylated flavonoids have been identified from plants. According to the number of prenylated flavonoids reported before, prenylated flavonones are the most common subclass and prenylated flavanols is the rarest sub-class. Even though natural prenylated flavonoids have been detected to have diversely structural characteristics, they have a narrow distribution in plants, which are different to the parent flavonoids as they are present almost in all plants. Most of prenylated flavonoids are found in the following families, including *Cannabaceae*, *Guttiferae*, *Leguminosae*, *Moraceae*, *Rutaceae* and *Umbelliferae*. *Leguminosae* and *Moraceae*, due to their consumption as fruits and vegetables, are the most frequently investigated families and many novel prenylated flavonoids have been explored. *Humulus lupulus* of the *Cannabaceae* include 8-prenylnaringenin and xanthohumol, which can play a role in the health benefits of beer.

The prenylated flavonoid can be incorporated through a hops extract, incorporated in a separately added extract, or added as a separate component of the oral care compositions disclosed herein.

Suitable prenylated flavonoids can have a particular octanol-water partitioning coefficient. The octanol-water partitioning coefficient can be used to predict the lipophilicity of a compound. Without wishing to being bound by theory, it is believed that compounds that fall within the ranges described herein will be able to enter and/or disrupt the primarily hydrophobic phospholipid bilayer that makes of the cell membrane of microorganisms. Thus, the octanol-water partitioning coefficient can be correlated to the antibacterial effect of prenylated flavonoids. Suitable prenylated flavonoids can have a log P of at least about 2, at least about 4, from about 2 to about 10, from about 4 to about 10, from about 4 to about 7, or from about 4 to about 7.

The oral care composition can comprise at least about 0.001%, from about 0.001% to about 5%, from about 0.01% to about 2%, from about 0.0001% to about 2%, or at least about 0.05% of prenylated flavonoid.

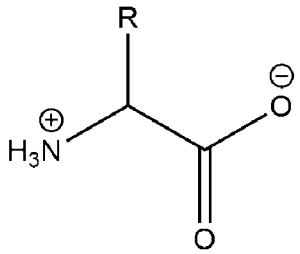
Amino Acid

The oral care composition can comprise amino acid. The amino acid can comprise one or more amino acids, peptide, and/or polypeptide, as described herein.

Amino acids, as in Formula XIV, are organic compounds that contain an amine functional group, a carboxyl functional group, and a side chain (R in Formula XIV) specific to each amino acid. Suitable amino acids include, for example, amino acids with a positive or negative side chain, amino acids with an acidic or basic side chain, amino acids with polar uncharged side chains, amino acids with hydrophobic side chains, and/or combinations thereof. Suitable amino acids also include, for example, arginine, histidine, lysine, aspartic acid, glutamic acid, serine, threonine,

asparagine, glutamine, cysteine, selenocysteine, glycine, proline, alanine, valine, isoleucine, leucine, methionine, phenylalanine, tyrosine, tryptophan, citrulline, ornithine, creatine, diaminobutanoic acid, diaminoproprionic acid, salts thereof, and/or combinations thereof.

Suitable amino acids include the compounds described by Formula XIV, either naturally occurring or synthetically derived. The amino acid can be zwitterionic, neutral, positively charged, or negatively charged based on the R group and the environment. The charge of the amino acid, and whether particular functional groups, can interact with tin at particular pH conditions, would be well known to one of ordinary skill in the art.



Formula XIV. Amino Acid. R is any suitable functional group

Suitable amino acids include one or more basic amino acids, one or more acidic amino acids, one or more neutral amino acids, or combinations thereof.

The oral care composition can comprise from about 0.01% to about 20%, from about 0.1% to about 10%, from about 0.5% to about 6%, or from about 1% to about 10 % of amino acid, by weight of the oral care composition.

The term "neutral amino acids" as used herein include not only naturally occurring neutral amino acids, such as alanine, asparagine, cysteine, glutamine, glycine, isoleucine, leucine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, valine, but also biologically acceptable amino acids which have an isoelectric point in range of pH 5.0 to 7.0. The biologically preferred acceptable neutral amino acid has a single amino group and carboxyl group in the molecule or a functional derivative hereof, such as functional derivatives having an altered side chain albeit similar or substantially similar physio chemical properties. In a further embodiment the amino acid would be at minimum partially water soluble and provide a pH of less than 7 in an aqueous solution of 1g/1000ml at 25 °C.

Accordingly, neutral amino acids suitable for use in embodiments of the present invention include, but are not limited to, alanine, aminobutyrate, asparagine, cysteine, cystine, glutamine, glycine, hydroxyproline, isoleucine, leucine, methionine, phenylalanine, proline, serine, taurine, threonine, tryptophan, tyrosine, valine, salts thereof, or mixtures thereof. Preferably, the neutral amino acids used in embodiments of the present invention may include asparagine, glutamine,

glycine, salts thereof, or mixtures thereof. The neutral amino acids may have an isoelectric point of 5.0, or 5.1, or 5.2, or 5.3, or 5.4, or 5.5, or 5.6, or 5.7, or 5.8, or 5.9, or 6.0, or 6.1, or 6.2, or 6.3, or 6.4, or 6.5, or 6.6, or 6.7, or 6.8, or 6.9, or 7.0, in an aqueous solution at 25 °C. Preferably, the neutral amino acid is selected from proline, glutamine, or glycine, more preferably in its free form (i.e., uncomplexed). If the neutral amino acid is in its salt form, suitable salts include salts known in the art to be pharmaceutically acceptable salts considered to be physiologically acceptable in the amounts and concentrations provided. Preferably the neutral amino acid is present in the amount of from about 0.0001% to about 10%, preferably from about 0.05% to about 5%, preferably from about 0.1% to about 3%, preferably from about 0.5% to about 3%, preferably from about 1% to about 3%, by weight of the composition. In one aspect, the neutral amino acid is glutamine (or salt thereof). In another aspect, the neutral amino acid is proline (or salt thereof). In yet another aspect, the neutral amino acid is glycine (or salt thereof).

The oral care composition can comprise from about 0.0001% to about 20%, from about 0.1% to about 10%, from about 0.5% to about 6%, or from about 1% to about 10 % of neutral amino acid, by weight of the oral care composition.

Whitening Agent

The oral care composition may comprise from about 0.1% to about 10%, from about 0.2% to about 5%, from about 1% to about 5%, or from about 1% to about 15%, by weight of the oral care composition, of a whitening agent. The whitening agent can be a compound suitable for whitening at least one tooth in the oral cavity. The whitening agent may include peroxides, metal chlorites, perborates, percarbonates, peroxyacids, persulfates, dicarboxylic acids, and combinations thereof. Suitable peroxides include solid peroxides, hydrogen peroxide, urea peroxide, calcium peroxide, benzoyl peroxide, sodium peroxide, barium peroxide, inorganic peroxides, hydroperoxides, organic peroxides, and mixtures thereof. Suitable metal chlorites include calcium chlorite, barium chlorite, magnesium chlorite, lithium chlorite, sodium chlorite, and potassium chlorite. Other suitable whitening agents include sodium persulfate, potassium persulfate, peroxydone, 6-phthalimido peroxy hexanoic acid, pthalamidoperoxycaproic acid, or mixtures thereof.

Humectant

The oral care composition can comprise one or more humectants, have low levels of a humectant, be essentially free of, be substantially free of, or be free of a humectant. Humectants serve to add body or "mouth texture" to an oral care composition or dentifrice as well as preventing

the dentifrice from drying out. Suitable humectants include polyethylene glycol (at a variety of different molecular weights), propylene glycol, glycerin (glycerol), erythritol, xylitol, sorbitol, mannitol, butylene glycol, lactitol, hydrogenated starch hydrolysates, and/or mixtures thereof. The oral care composition can comprise one or more humectants each at a level of from 0 to about 70%, from about 5% to about 50%, from about 10% to about 60%, or from about 20% to about 80%, by weight of the oral care composition.

Water

The oral care composition according to embodiments of the present invention can be anhydrous, a low water formulation, or a high water formulation. In total, the oral care composition can comprise from 0% to about 99%, from about 5% to about 75%, about 20% or greater, about 30% or greater, about 50% or greater, up to about 45%, or up to about 75%, by weight of the composition, of water.

In a high water oral care composition and/or toothpaste formulation, the oral care composition comprises from about 45% to about 75%, by weight of the composition, of water. The high water oral care composition and/or toothpaste formulation can comprise from about 45% to about 65%, from about 45% to about 55%, or from about 46% to about 54%, by weight of the composition, of water. The water may be added to the high water formulation and/or may come into the composition from the inclusion of other ingredients.

In a low water oral care composition and/or toothpaste formulation, the oral care composition comprises from about 5% to about 45%, by weight of the composition, of water. The low water oral care composition can comprise from about 5% to about 35%, from about 10% to about 25%, or from about 20% to about 25%, by weight of the composition, of water. The water may be added to the low water formulation and/or may come into the composition from the inclusion of other ingredients.

In an anhydrous oral care composition and/or toothpaste formulation, the oral care composition comprises less than about 10%, by weight of the composition, of water. The anhydrous composition comprises less than about 5%, less than about 1%, or 0%, by weight of the composition, of water. The water may be added to the anhydrous formulation and/or may come into the composition from the inclusion of other ingredients.

The oral care composition can also be a mouth rinse formulation. A mouth rinse formulation can comprise from about 75% to about 99%, from about 75% to about 95%, or from about 80% to about 95% of water.

The dentifrice composition can also comprise other orally acceptable carrier materials, such

as alcohol, humectants, polymers, surfactants, and acceptance improving agents, such as flavoring, sweetening, coloring and/or cooling agents.

Other Ingredients

The oral care composition can comprise a variety of other ingredients, such as flavoring agents, sweeteners, colorants, preservatives, buffering agents, or other ingredients suitable for use in oral care compositions, as described below.

Flavoring agents also can be added to the oral care composition. Suitable flavoring agents include oil of wintergreen, oil of peppermint, oil of spearmint, clove bud oil, menthol, anethole, methyl salicylate, eucalyptol, cassia, 1-menthyl acetate, sage, eugenol, parsley oil, oxanone, alpha-irisone, marjoram, lemon, orange, propenyl guaethol, cinnamon, vanillin, ethyl vanillin, heliotropine, 4-cis-heptenal, diacetyl, methyl-para-tert-butyl phenyl acetate, and mixtures thereof. Coolants may also be part of the flavor system. Preferred coolants in the present compositions are the paramenthan carboxyamide agents such as N-ethyl-p-menthan-3-carboxamide (known commercially as "WS-3") or N-(Ethoxycarbonylmethyl)-3-p-menthanecarboxamide (known commercially as "WS-5"), and mixtures thereof. A flavor system is generally used in the compositions at levels of from about 0.001 % to about 5%, by weight of the oral care composition. These flavoring agents generally comprise mixtures of aldehydes, ketones, esters, phenols, acids, and aliphatic, aromatic and other alcohols.

Sweeteners can be added to the oral care composition to impart a pleasing taste to the product. Suitable sweeteners include saccharin (as sodium, potassium or calcium saccharin), cyclamate (as a sodium, potassium or calcium salt), acesulfame-K, thaumatin, neohesperidin dihydrochalcone, ammoniated glycyrrhizin, dextrose, levulose, sucrose, mannose, sucralose, stevia, and glucose.

Colorants can be added to improve the aesthetic appearance of the product. Suitable colorants include without limitation those colorants approved by appropriate regulatory bodies such as the FDA and those listed in the European Food and Pharmaceutical Directives and include pigments, such as TiO_2, and colors such as FD&C and D&C dyes.

Preservatives also can be added to the oral care compositions to prevent bacterial growth. Suitable preservatives approved for use in oral compositions such as methylparaben, propylparaben, benzoic acid, and sodium benzoate can be added in safe and effective amounts.

Titanium dioxide may also be added to the present composition. Titanium dioxide is a white powder which adds opacity to the compositions. Titanium dioxide generally comprises from about 0.25% to about 5%, by weight of the oral care composition.

Other ingredients can be used in the oral care composition, such as desensitizing agents, healing agents, other caries preventative agents, chelating/sequestering agents, vitamins, amino acids, proteins, other anti-plaque/anti-calculus agents, opacifiers, antibiotics, anti-enzymes, enzymes, pH control agents, oxidizing agents, antioxidants, and the like.

Oral Care Composition Forms

Suitable compositions forms include emulsion compositions, such as the emulsions compositions of U.S. Patent No. 11,147,753, which is herein incorporated by reference in its entirety, unit-dose compositions, such as the unit-dose compositions of U.S. Patent Application Publication No. 2019/0343732, which is herein incorporated by reference in its entirety, leave-on oral care compositions, jammed emulsions, such as the jammed oil-in-water emulsions of U.S. Patent No. 11,096,874, which is herein incorporated by reference in its entirety, dentifrice compositions, mouth rinse compositions, mouthwash compositions, tooth gel, subgingival gel, mouth rinse, mousse, foam, mouth spray, lozenge, chewable tablet, chewing gum, tooth whitening strips, floss and floss coatings, breath freshening dissolvable strips, denture care products, denture adhesive products, or combinations thereof.

Methods

The oral care compositions, as described herein, can lead to oral health benefits, such as the treatment, reduction, and/or prevention of caries, cavities, gingivitis, and/or combinations thereof and/or the whitening of teeth, removing stain from teeth, and/or preventing the accumulation of stain from teeth when applied to the oral cavity. For example, a user can dispense at least a one-inch strip of a suitable oral care composition, as described herein, onto an oral care implement, such as a toothbrush, applicator, and/or tray, and applied to the oral cavity and/or teeth.

The user can be instructed to brush teeth thoroughly for at least 30 seconds, at least one minute, at least 90 seconds, or at least two minutes at least once, at least twice, or at least three times per day. The user can also be instructed to expectorate the oral care composition after the completion of the brush procedure.

The user can also be instructed to rinse with a mouthwash and/or mouth rinse composition after the completion of the brush procedure or instead of the brush procedure. The user can be instructed to swish the oral care composition thoroughly for at least 30 seconds, at least one minute, at least 90 seconds, or at least two minutes at least once, at least twice, or at least three times per day. The user can also be instructed to expectorate the oral care composition after the completion of the procedure.

The oral care compositions according to embodiments of the present invention can be used in the treatment, reduction, and/or prevention of caries, cavities, gingivitis, and/or combinations thereof. The oral care compositions according to embodiments of the present invention can be used to provide a whitening benefit, such as the whitening of teeth, removing stain from teeth, and/or preventing the accumulation of stain from teeth. For example, as described herein, hops beta acid can be useful as an antigingivitis agent. Thus, the addition of hops to any oral care composition can provide antigingivitis protection.

The oral care composition can include primary packaging, such as a tube, bottle, and/or tub. The primary package can be placed within secondary package, such as a carton, shrink wrap, or the like. Instructions for use of the oral care composition can be printed on the primary package and/or the secondary package. The scope of the method is intended to include instructions provided by a manufacturer, distributor, and/or producer of the oral care composition.

If the oral care composition is a toothpaste, the user can be instructed to dispense the toothpaste from the toothpaste tube.

The user can be instructed to apply a portion of the toothpaste onto a toothbrush. The portion of the toothpaste can be of any suitable shape, such as strip, a pea-sized amount, or various other shapes that would fit onto any mechanical and/or manual brush head. The user can be instructed to apply a strip of the toothpaste that is at least about 1 inch, at least about 0.5 inch, at least 1 inch, and/or at least 0.5 inch long to the bristles of a toothbrush, such as soft-bristled toothbrush.

The user can be instructed to apply pea-sized or grain of rice-sized portion of the toothpaste to the bristles of a toothbrush, such as in the case of use by children of less than 6 years old and/or less than 2 years old.

The user can be instructed to brush their teeth for at least about 30 seconds, at least about 1 minute, at least about 90 seconds, at least about 2 minutes, at least 30 seconds, at least 1 minute, at least 90 seconds, and/or at least 2 minutes.

The user can be instructed to brush their teeth thoroughly and/or as directed by a physician and/or dentist.

The user can be instructed to brush their teeth after each meal. The user can be instructed to brush their teeth at least once per day, at least twice per day, and/or at least three times per day. The user can be instructed to brush their teeth no more than three times a day, such as to prevent Sn staining. The user can be instructed to brush their teeth in the morning and/or in the evening prior to sleeping.

The user can be instructed to not swallow the toothpaste composition due to the inclusion of ingredients that are not suitable for ingestion, such as fluoride. However, in the case of an oral care composition comprising hops, but free of fluoride, the user may not need to be instructed to not swallow the toothpaste. The user may be instructed to expectorate (or spit out) the toothpaste composition after the cessation of the brushing cycle.

If the oral care composition is a mouth rinse, the user can be instructed to dispense the mouth rinse from a bottle containing the mouth rinse.

The user can be instructed to use the mouth rinse at least once a day, at least twice a day, and/or at least three times a day.

The user can be instructed to use the mouth rinse composition after the use of toothpaste and/or floss.

The user can be instructed to swish a portion of rinse in the oral cavity, such as between the teeth, for a period of time. The user can be instructed to vigorously swish a portion of the rinse.

The user can be instructed to use be from about 5 mL to about 50 mL, from about 10 mL to about 40 mL, 10 mL, 20 mL, 25 mL, 30 mL, 40 mL, 2 teaspoonfuls, and/or 4 teaspoonfuls of mouth rinse.

The user can be instructed to swish the mouth rinse for at least about 30 seconds, at least about 1 minute, at least about 90 seconds, at least about 2 minutes, at least 30 seconds, at least 1 minute, at least 90 seconds, and/or at least 2 minutes.

The user can be instructed to not swallow the mouth rinse composition due to the inclusion of ingredients that are not suitable for ingestion, such as fluoride. However, in the case of an oral care composition comprising hops, but free of fluoride, the user may not need to be instructed to not swallow the mouth rinse. The user may be instructed to expectorate (or spit out) the mouth rinse composition after the cessation of the rinse cycle.

The usage instructions for the oral care composition, such as for a toothpaste composition and/or a mouth rinse composition, can vary based on age. For example, adults and children that are at least 6 or at least 2 can have one usage instruction while children under 6 or under 2 can have a second usage instruction.

The oral care composition comprising hops, as described herein, can be useful as medicament, such as in an anticavity and/or antigingivitis treatment, as described herein. Suitable medicaments include oral care compositions, toothpaste compositions, mouth rinse compositions, floss coatings, chewing gums, and/or other suitable compositions to be applied in the oral cavity.

Additionally, the oral care composition, as described herein, can be used to reduce the

number and/or intensity of white spots on teeth, which can be attributable to caries presence within the oral cavity. Or the oral care composition, as described herein, can be used to reduce the redness, puffiness, tenderness, and/or swollenness of gums at the gumline immediately adjacent the surfaces of the teeth, which can be attributable to gingivitis presence within the oral cavity.

COMBINATIONS

A. An oral care composition comprising hops acid; about 1 to about 1,000 μg per gram of the oral care composition of residual iron; and a stabilization system comprising an iron metal ion chelate, where the iron metal ion chelate comprises a polydentate polyphosphate having at least two functional groups, a polycarboxylate having at least three carboxylate groups, or a combination thereof.

B. The oral care composition as disclosed in A, where the iron metal ion chelate has an affinity for ferrous (II) or ferric (III) iron ions, preferably where the iron metal ion chelate is an iron (II) metal ion chelate having a log K1 greater than about 2 or is an iron (III) metal ion chelate having a log K1 greater than about 10.

C. The oral care composition as disclosed in A or B, where the composition has an improved color stability compared to a control without the stabilization system.

D. The oral care composition as disclosed in A-C, where the composition is free of a stannous ion source.

E. The oral care composition as disclosed in A-C, further comprising a stannous ion source.

F. The oral care composition as disclosed in A-E, where the iron metal ion chelate comprises the polydentate polyphosphate, and the polydentate polyphosphate comprises pyrophosphate.

G. The oral care composition as disclosed in A-F, where the iron metal ion chelate comprises the polydentate polyphosphate, and the polydentate polyphosphate comprises phytate.

H. The oral care composition as disclosed in A-G, where the iron metal ion chelate comprises the polycarboxylate, and the polycarboxylate comprises citrate.

I. The oral care composition as disclosed in A-H, where the iron metal ion chelate comprises the polycarboxylate, and the polycarboxylate comprises zinc citrate.

J. The oral care composition as disclosed in A-I, where the iron metal ion chelate comprises the polycarboxylate, and the polycarboxylate comprises sodium citrate.

K. The oral care composition as disclosed in H-J, where the stabilization system further comprises gluconate.

L. The oral care composition as disclosed in A-K, further comprising an abrasive.

M. The oral care composition as disclosed in L, where the abrasive comprises calcium abrasive.

N. The oral care composition as disclosed in M, where the calcium abrasive comprises calcium carbonate.

O. The oral care composition as disclosed in A-N, where the oral care composition is free of silica.

P. The oral care composition as disclosed in A-O, where the oral care composition is free of fluoride.

Q. The oral care composition as disclosed in A-P, further comprising a fluoride ion source.

R. The oral care composition as disclosed in A-Q, further comprising from about 0.01% to about 10%, by weight of the composition, of a metal ion source.

S. The oral care composition as disclosed in R, where the metal ion source comprises a zinc ion source.

T. The oral care composition as disclosed in A-S, where the hops beta acid comprises only non-hydrogenated hops beta acid.

U. The oral care composition as disclosed in A-T, where the oral care composition comprises from about 0.05% to about 10%, preferably from about 0.05% to about 5%, or more preferably from about 0.05% to about 2%, by weight of the composition, of the hops beta acid.

V. The oral care composition as disclosed in A-U, where the oral care composition comprises from about 0.1% to about 10%, preferably from about 0.1% to about 5%, or more preferably from about 1% to about 4%, by weight of the composition, of the stabilization system.

W. The oral care composition as disclosed in A-V, where an addition of the stabilization system results in:

a change in L* (ΔL) compared to the composition without the stabilization system of from about -5 to about 25, preferably about -3 to about 25, more preferably about -1 to about 25, or most preferably about 0 to about 25; and/or

a change in a* (Δa) compared to the composition without the stabilization system of from about -5 to about 1, or preferably about -5 about 0; and/or

a change in b* (Δb) compared to the composition without the stabilization system of, for example, from about -20 to about 0, or more preferably about -25 about 0.

X. The oral care composition as disclosed in A-W, where the stabilization system further comprises EDTA.

EXAMPLES

The invention is further illustrated by the following examples, which are not to be construed in any way as imposing limitations to the scope of this invention. Various other aspects, modifications, and equivalents thereof which, after reading the description herein, may suggest themselves to one of ordinary skill in the art without departing from the spirit of the present invention or the scope of the appended claims.

TABLE 1 describes the hops beta acid extract provided by Hopsteiner®, which is used in the compositions of TABLES 2, 3, 4A, 4B, and 5. Since the hops beta acids are provided as an extract, there can be some variability in the amounts of certain ingredients. However, the extract comprises approximately 45%, by weight of the extract, of hops beta acids and approximately 0.4%, by weight of the extract, of hops alpha acids. This is different to traditional hops extracts which typically have more hops alpha acids than hops beta acids. Other minor ingredients may be present in the Hops Beta Acid extract.

TABLE 1. Hops Beta Acids Extract Specification

Ingredient	Amount (wt%)
Hops Beta Acids	45 ± 2
Hops Alpha Acids	0.4 ± 0.3
Hops oils	1.5 ± 0.5
Propylene Glycol	20 ± 15
Water	< 8%
pH	11 ± 0.5

Effect of Stabilization Systems on Color Stability

The oral care compositions of TABLES 2, 3, 4A, 4B, and 5 were prepared by combining one or more humectants, water, sweetener(s), and metal salts, buffers, dyes, and/or stabilizing agents to create a liquid mixture. The liquid mixture was homogenized at 25 °C until homogeneous and completely dissolved. Next, sodium hydroxide (50% solution) was added to the liquid mixture and the liquid mixture was homogenized at 25 °C until homogeneous and completely dissolved. A separate powder mixture was prepared by combining the abrasive silica, thickening silica, and opacifier, with any thickening agents, such as xanthan gum, GANTREZ, and/or sodium carboxymethylcellulose. The powder mixture was then combined with the liquid mixture and homogenized completely. Next, the surfactant, such as sodium lauryl sulfate, flavor, and hops extract were added to the mixture. The contents were homogenized at 25 °C until homogeneous, and entrained air was removed by vacuum. The stabilization system in Ex. 1, as shown in TABLE 2, includes gluconate and lactate.

TABLE 2. Oral Care Composition

Ingredient (wt%)	Ex. 1
Stannous Fluoride	0.454
USP Water	25.500
Sorbitol Solution (70%)	37.452
GANTREZ S-95	5.710
Zinc Lactate	0.250
Sodium Gluconate	1.064
Sodium Saccharin	0.800
Dental Silica	15.000
Hydroxyethyl Cellulose	0.720
Carrageenan	1.080
Xanthan Gum	0.540
Xylitol	3.000
Sodium Lauryl Sulfate Solution (27.9%)	5.000
Sodium Hydroxide Solution (50%)	1.200
Hops Beta Acids Extract	0.330
Titanium Dioxide	0.500
Flavor	1.200
Dye Solution FD&C Blue #1	0.200

FIGS. 1A and 1B show the color of Ex. 1 following storage in a toothpaste tube at 40 °C for one month. The composition in TABLE 2, Ex. 1, has an ineffective stabilization system based upon monodentate ligands only, gluconate and lactate. This stabilization system allowed for significant tip discoloration in the presence of iron and a hops beta acid extract. As shown in FIGS. 1A and 1B, the left-most area of paste is a darker color compared to the right-most paste. The dark discoloration of the paste that was stored at the tip (left-most paste) is related in part to the formation of a complex of hops beta acid with iron because of insufficient chelation of residual soluble iron in the formula.

The compositions in TABLE 3 vary with respect to their iron and stabilizer content. Ex. 2A is the control composition that contains a gluconate/citrate stabilization system along with silica. Silica may bring a significant amount of residual soluble iron due to its nature. Additionally, during processing, silica can abrade stainless-steel production equipment thus increasing the iron content of the toothpaste.

TABLE 3. Oral Care Compositions

	Control	No Sn/Silica	No Silica	No Citrate/Gluconate
Ingredient (wt%)	Ex. 2A	Ex. 2B	Ex. 2C	Ex. 2D
Sorbitol Solution (70%)	48.000	48.000	48.000	48.000
Treated Water	19.581	38.097	37.081	22.464
SnF_2	0.454	0	0.454	0.454
$SnCl_2$ 10% silica blend	0.562	0	0.562	0.562
Sodium Gluconate	1.300	1.300	1.300	0
NaOH (50%)	0.870	0.870	0.870	0.870
Saccharin	0.400	0.400	0.400	0.400
Sucralose (25%)	0.200	0.200	0.200	0.200
Xanthan Gum	0.875	0.875	0.875	0.875
Carrageenan	1.500	1.500	1.500	1.500
Zinc Citrate	0.533	0.533	0.533	0
Sodium Citrate	1.050	1.050	1.050	0
TiO_2	0.500	0.500	0.500	0.500
Silica	17.500	0	0	17.500
SLSS (29%)	5.000	5.000	5.000	5.000
Hops Beta Acids Extract	0.500	0.500	0.500	0.500
Flavor	1.175	1.175	1.175	1.175

FIGS. 2A and 2B show the color of Examples 2A-2D after storage in a toothpaste tube at room temperature (about 20 °C) for seven days. Residual iron from the silica and manufacturing process led to slight discoloration of the tip in Ex. 2A as compared to a no Sn^{2+}/no silica composition, Ex. 2B, or a no silica composition, Ex. 2C. When the stabilizers were removed from the composition, Ex. 2D, then the discoloration was extreme. Unlike the combination of gluconate and lactate in Ex. 1, the combination of gluconate and citrate is an effective chelation system to manage the discoloration of the hops beta acid extract in the presence of iron. If the silica is removed from the composition, as in Ex. 2C, the tip darkening with respect to the control product, Ex. 2A, was less pronounced. When the Sn^{2+} and silica were removed from the composition as in Ex. 2B, the tip darkening with respect to the control product, Ex. 2A, was even less pronounced because more of the gluconate/citrate stabilization system was available to chelate the iron without the presence of a competing Sn^{2+} cation. When, however, the gluconate/citrate stabilization system was removed (Ex. 2D), the tip darkening was pronounced as illustrated in FIGS. 2A and 2B.

Tables 4A, 4B, and 5 include various dentifrice compositions without binder (for ease of separation of solid and liquid components) including various stabilizers and a control (Ex. 3A)

with no stabilizer.

TABLE 4A. Oral Care Compositions

Ingredient (wt%)	Ex. 3A	Ex. 3B	Ex. 3C	Ex. 3D	Ex. 3E	Ex. 3F	Ex. 3G	Ex. 3H
Sorbitol Solution (70%)	48.000	48.000	48.000	48.000	48.000	48.000	48.000	48.000
Treated Water	26.450	25.350	23.400	25.000	26.050	25.900	23.150	25.350
SnF_2	0.450	0.450	0.450	0.450	0.450	0.450	0.450	0.450
$SnCl_2$ 10% silica blend	0.550	0.550	0.550	0.550	0.550	0.550	0.550	0.550
NaF	0.100	0.100	0.100	0.100	0.100	0.100	0.100	0.100
NaOH (50%)	0.850	0.850	0.850	0.850	0.850	0.850	0.850	0.850
Saccharin	0.400	0.400	0.400	0.400	0.400	0.400	0.400	0.400
Sucralose (25%)	0.200	0.200	0.200	0.200	0.200	0.200	0.200	0.200
Xanthan Gum	0	0	0	0	0	0	0	0
Carrageenan	0	0	0	0	0	0	0	0
TiO_2	0	0	0	0	0	0	0	0
Silica	17.500	17.500	17.500	17.500	17.500	17.500	17.500	17.500
SLSS (29%)	5.000	5.000	5.000	5.000	5.000	5.000	5.000	5.000
Hops Beta Acids Extract	0.500	0.500	0.500	0.500	0.500	0.500	0.500	0.500
Flavor	0	0	0	0	0	0	0	0
Sodium Acid Pyrophosphate Anhydrous	0	1.100	0	0	0	0	0	0
Zinc Citrate Dihydrate	0	0	3.05	0	0	0	0	0
Sodium Citrate Dihydrate	0	0	0	1.450	0	0	0	0
Sodium Bicarbonate	0	0	0	0	0.400	0	0	0
Sodium Carbonate (Anh)	0	0	0	0	0	0.550	0	0
Sodium Phytate	0	0	0	0	0	0	3.300	0
Sodium Gluconate	0	0	0	0	0	0	0	1.100
Total	100	100	100	100	100	100	100	100
pH final adjustment	6.8	6.8	6.8	6.8	6.8	6.8	6.8	6.8

TABLE 4B. Oral Care Compositions

Ingredient (wt%)	Ex. 3I	Ex. 3J
Sorbitol Solution (70%)	48.000	48.000
Treated Water	24.300	24.300
SnF_2	0.450	0.450
$SnCl_2$ 10% silica blend	0.550	0.550
NaF	0.100	0.100
NaOH (50%)	0.850	0.850
Saccharin	0.400	0.400
Sucralose (25%)	0.200	0.200
Xanthan Gum	0	0
Carrageenan	0	0
TiO_2	0	0
Silica	17.500	17.500
SLSS (29%)	5.000	5.000
Hops Beta Acids Extract	0.500	0.500
Flavor	0	0
Sodium Tripolyphosphate, Pentasodium	7.500	0
Sodium Hexametaphosphate, Glass H	0	7.500
Total	100	100
pH final adjustment	6.8	6.8

TABLE 5. Oral Care Compositions

Ingredient (wt%)	Ex. 4A	Ex. 4B	Ex. 4C	Ex. 4D	Ex. 4E	Ex. 4F
Treated Water	8.579	8.570	8.557	8.535	8.492	8.408
Sorbitol Solution (70%)	35.236	35.200	35.146	35.058	34.881	34.533
Glycerin USP	27.230	27.203	27.161	27.092	26.956	26.687
$SnCl_2$ 10% silica blend	0.447	0.447	0.446	0.445	0.443	0.439
SnF_2	0.462	0.461	0.461	0.459	0.457	0.452
Sodium Citrate Dihydrate	1.403	1.402	1.400	1.396	1.389	1.375
Sodium Gluconate	1.042	1.041	1.040	1.037	1.032	1.022
NaOH (50%)	0.732	0.731	0.730	0.728	0.725	0.718
Silica	15.254	15.238	15.215	15.176	15.100	14.950
Saccharin	0.508	0.508	0.507	0.506	0.503	0.498
Sucralose (25%)	0.163	0.163	0.162	0.162	0.161	0.159
Hops Beta Acids Extract	0.508	0.508	0.507	0.506	0.503	0.498
EDTA	0.000	0.102	0.254	0.506	1.007	1.993
SLSS (29% Sol)	5.720	5.714	5.706	5.691	5.663	5.606
Cocamidopropyl Betaine (30% Sol)	1.525	1.524	1.521	1.518	1.510	1.495
Flavor	1.190	1.189	1.187	1.184	1.178	1.166
Total	100	100	100	100	100	100
pH final adjustment	6.8	6.8	6.8	6.8	6.8	6.8

Color Measurement Method

The toothpaste samples of the examples in TABLES 4A, 4B, and 5 were all kept in polypropylene tubes at room temperature (20 °C) for 5 or 7 days before being tested by a colorimeter. The L*a*b* values of Examples 3B-3J were compared with that of Ex. 3A to assess the improvement of color stability by the stabilization system (i.e., chelate addition).

After aging, each toothpaste sample was centrifuged at 15000 rpm for 10 min to separate the insoluble portion. The supernatant was filled up in quartz dish (20 mm dia., 3 mm dpt.) and measured for L*a*b* value using X-rite Model VS3200 Colorimeter. In L*a*b* color space, "L" represents darkness to lightness, with values ranging from 0 to 100; "a" represents greenness to redness with values of -128 to +127; and "b" represents blueness to yellowness also with values from -128 to +127. An improvement on color stability in comparison to the comparative Ex. 3A was determined to be a positive ΔL, negative Δa, and negative Δb.

TABLE 6A. Color Change of Oral Care Compositions vs. Ex. 3A

	Ex. 3A	Ex. 3B	Ex. 3C	Ex. 3D	Ex. 3E	Ex. 3F	Ex. 3G	Ex. 3H
ΔL	-	2.12	4.75	12.76	0.99	6.86	11.25	0.82
Δa	-	-0.52	-1.60	-1.74	1.67	0.28	-1.68	0.33
Δb	-	-2.26	-8.74	-20.78	-5.38	-12.62	-18.72	-0.25

Day of Measurement	5 & 7	7	7	7	7	7	7	7

TABLE 6B. Color Change in Oral Care Compositions vs. Ex. 3A

	Ex. 3I	Ex. 3J
ΔL	4.97	3.45
Δa	-1.28	-0.81
Δb	-5.72	-3.49
Day of Measurement	5	7

The compositions in TABLES 4A and 4B were assessed by colorimetry for their L*a*b* color values. The results are shown in TABLES 6A and 6B. FIGS. 3A and 3B show the results of Examples 3A-3H. Those compositions that are ineffectively stabilized toward residual soluble iron become darkly discolored. The difference was calculated vs. the control sample, Ex. 3A. The systems with a positive ΔL, negative Δa, and negative Δb relative to the control sample demonstrated an effective stabilization system towards discoloration in the presence of iron and a hops beta acid extract. The most effective stabilizers were those used in compositions that showed large positive ΔL and large negative Δa and Δb values. These effective stabilizers included sodium acid pyrophosphate (Ex. 3B), zinc citrate (Ex. 3C), sodium citrate (Ex. 3D), sodium phytate (Ex. 3G), sodium tripolyphosphate pentasodium (Ex. 3I), and sodium hexametaphosphate (Glass H) (Ex. 3J). Without wishing to be bound by theory, polydentate polyphosphate ($n > 2$) and polycarboxylate ($n > 3$) stabilization systems appear to adequately prevent the discoloration of a hops beta acid extract in the presence of residual soluble iron. The stabilization systems including only sodium bicarbonate (Ex. 3E), sodium carbonate (Ex. 3F), or gluconate (Ex. 3H) were not able to adequately prevent the discoloration of a hops beta acid extract in the presence of residual soluble iron.

TABLE 7. Color Change in Oral Care Compositions vs. Ex. 3A

	Ex. 3A	Ex. 4A	Ex. 4B	Ex. 4C	Ex. 4D	Ex. 4E	Ex. 4F
ΔL	-	11.84	12.99	13.04	12.94	13.52	11.34
Δa	-	-1.80	-1.80	-1.81	-1.69	-1.63	-1.38
Δb	-	-21.00	-21.65	-21.69	-22.45	-22.76	-24.04
Day of Measurement	7	7	7	7	7	7	7

The compositions in TABLE 5 were evaluated to determine the impact of EDTA in addition to citrate as a stabilization system for hops against color change through metal chelation. Sodium citrate (Ex. 3D) was shown to be an effective stabilizer against this color change. Further addition of EDTA improved the stability of the composition towards color change as especially observed

in the further reduction of the b* color value as illustrated in TABLE 7. All compositions containing EDTA (Ex. 4B, 4C, 4D, 4E, and 4F) improved the color of the compositions already containing sodium citrate. Without wishing to be bound by theory, it is believed that EDTA would work in combination with citrate or on its own to reduce the color change caused by the interaction between hops and iron.

Effect of Pyrophosphate on Hops Stability in the Bulk of the Toothpaste Tube

To demonstrate pyrophosphate effects on hops stability, a series of products were made that contained varying amounts of a hops beta acid extract in a toothpaste that did not contain pyrophosphate (Crest Cavity Protection) and a toothpaste that contained approximately 3% sodium acid pyrophosphate, anhydrous (Crest Complete Extra Whitening). The ingredients of Crest Cavity Protection and Crest Complete Extra Whitening are shown in TABLE 8. Both toothpaste bases include sodium fluoride and silica and do not include a stannous ion source.

After combining hops with each toothpaste base, samples were then filled into tubes and placed on stability at 40 °C at 75% Relative Humidity. Samples were pulled at the times indicated in TABLE 9 and allowed to equilibrate to room temperature. Approximately 5 g were dispensed to obtain a sample from the bulk of the toothpaste tube. After appropriate dilutions in a 1:1 water:methanol mixture, toothpaste samples were then analyzed for the amount of remaining hops acid by measuring UV absorbance at 366 nm.

TABLE 8. Oral Care Compositions

Crest Cavity Protection	Crest Complete Extra Whitening
Sorbitol	Sorbitol
Water	Water
Dental Silica	Dental Silica
Sodium Lauryl Sulfate	Sodium Lauryl Sulfate
Trisodium Phosphate	Sodium Acid Pyrophosphate
Sodium Phosphate	Sodium Hydroxide
Cellulose Gum	Xanthan Gum
Carbomer	Cellulose gum
Sodium Saccharin	Carbomer
Titanium Dioxide	Titanium Dioxide
Dye	Dye
Sodium Fluoride	Sodium Fluoride
	Sodium Saccharin
	Polyethylene

TABLE 9. Effect of Pyrophosphate on Hops Stability in Different Toothpaste Bases

Example	Toothpaste Base	Hops Extract (wt%)	% Hops Beta Acid Remaining After Storage		
			45 days	90 days	180 days
5A	Crest Cavity Protection	0.55	76	55	27
5B	Crest Complete Extra Whitening	0.55	89	91	77
5C	Crest Cavity Protection	1.11	83	80	31
5D	Crest Complete Extra Whitening	1.11	100	89	91

Pyrophosphate anion has been shown in previous examples to bind the soluble iron that would otherwise interact with the hops acid to form an off color. The same complexation of residual iron in the tube extended the shelf stability of the hops acid in the pyrophosphate-containing toothpaste base (Ex. 5B and Ex. 5D) vs. a pyrophosphate-placebo toothpaste base (Ex. 5A and Ex. 5C). Without wishing to be bound by theory, those agents that prevent the color change caused by the iron-hops acid interaction are believed to also improve the stability of hops acid in the bulk of a toothpaste tube. Pyrophosphate was observed to both reduce the hops-iron darkening and improve the hops acid shelf life in a pyrophosphate-containing toothpaste base.

TABLE 10 describes the Hops Alpha and Beta Acids Extract provided by Hopsteiner®, which is used in the compositions of TABLE 11. Since the hops alpha and beta acids are provided as an extract, there can be some variability in the amounts of certain ingredients. However, the extract comprises approximately 70%, by weight of the extract, of the hops alpha and beta acids apportioned between alpha acid (39.8%) and beta acid (13.5%). This is different than the beta acid enriched extract described in TABLE 1 and more similar to traditional hops extracts, which typically have more hops alpha acids than hops beta acids. Other minor ingredients may be present in the Hops Alpha and Beta Acids Extract.

TABLE 10. Hops Alpha and Beta Acids Extract Specification

Ingredient	Amount (wt%)
Hops Beta Acids	18.4
Hops Alpha Acids	32.3
Hops Oils	3 – 12
Water	< 8%
Ethanol	Balance
pH	4.0 ± 0.5

The Hops Alpha and Beta Acids Extract of TABLE 10 was combined with commercially available Crest Cavity Protection (TABLE 8) and Crest Tartar Control (TABLE 13B) using a non-aerating, high-shear technique. Once combined, the compositions were sealed to air and allowed to sit at room temperature for two days. Following aging under these conditions, about 0.5 g of each composition, as well as its placebo base, was dispensed onto a glass slide then pressed into a disc approximately 2.0 mm thick using a second glass slide. The glass slide was placed onto a bright white surface (10 stacked white filter papers, Whatman #4 Qualitative Circles, Whatman International Ltd, Maidstone, England) and the color was determined in the CIELAB color space by holding a colorimeter (Color Reader CR-20, Konica Minolta, Inc., Tokyo, Japan) firmly against the top glass slide. The change in L*a*b* color value for each hops-containing product with respect to its placebo was calculated. The color of Crest Cavity Protection and Crest Tartar Control is similar but not exactly the same, so an average color value was determined by taking the mean L*a*b* color value and an adjusted, color-matched value was calculated for the starting products. L*a*b* values of the hops-containing versions were then determined based on the change in L*a*b* color originally determined. FIG. 4 shows the color of the adjusted starting products and the final colors of the products. Additionally, it shows the color of the Hops Alpha and Beta Acids Extract.

The darkening because of the hops-Fe interaction is observable in the color change of the adjusted Crest Cavity Protection (CCP*) from before to after the addition of the Hops Alpha and Beta Acids Extract (Hops αβ) with two days of aging in comparison to the color change of the adjusted Crest Tartar Protection (CTC*) from before to after addition of the extract with two days of aging. The pyrophosphate in Crest Tartar Control appeared to prevent or reduce this color change as evidenced by the smaller color change relative to its adjusted placebo. The color of Crest Tartar Control with the Hops Alpha and Beta Acids Blend is more similar to the base Crest Tartar Control.

The final colors of the hops-containing products and the adjusted base color are given in TABLE 11. The colors in TABLE 11 are also represented in FIG. 4.

TABLE 11. Color Change of Hops Alpha and Beta Acids Extract in Toothpaste

Example	Composition	Hops Alpha and Beta Acids Extract (%)	L*	a*	b*
-	Hops αβ Extract	100	36.6	8.5	33.7
-	Adjusted Base Color	0.00	77.45	-11.05	-3.35

Ex. 6A	Crest Cavity Protection*	1.00	71.75	-13.75	14.05
Ex. 6B	Crest Tartar Control*	1.00	77.05	-17.75	10.35

The Crest Cavity Protection with Hops Extract (Ex. 6A) has a lower L* value indicating an overall darkening of the material consistent with the purported mechanism of action for color change. The a* and b* values for Ex. 6A are also more consistent with a yellower and greener material than that for the Crest Tartar Control with the Hops Extract (Ex. 6B). The L*, a*, and b* color values for Ex. 6B are consistent with a brighter and more blue/green product than Ex. 6A. In general, the same prevention of darkening that was observed for the Hops Beta Acid Extract was also observed for the Hops Alpha and Beta Acid Extract.

Toothpastes can have a range of color values appropriate to communicate the content and action of the toothpaste to the consumer using the toothpaste. The color value of a selection of commercially obtained toothpastes were determined and are given in TABLE 12.

TABLE 12. CIELAB Color Values of Commercially Obtained Toothpastes

Toothpaste	Manufacturer	L*	a*	b*
Crest Cavity Protection Regular Paste	Procter & Gamble Cincinnati, OH	79.8	-13.7	-7.1
Crest Tartar Control Regular Paste	Procter & Gamble Cincinnati, OH	73.5	-14.1	-5.8
Crest 3D White Radiant Mint	Procter & Gamble Cincinnati, OH	59.5	-7.9	-7.6
Colgate Total Advanced Whitening	Colgate-Palmolive New York, NY	84.5	-1.2	1.5
Elmex Anti-Caries Professional	Colgate-Palmolive Świdnica, Poland	86.6	-1.1	6.3
Crest ProHealth Sensitive and Enamel Shield	Procter & Gamble Cincinnati, OH	67.1	-26.7	-12.4
Crest ProHealth Advanced Gum Protection	Procter & Gamble Cincinnati, OH	46.9	-26.4	-17.4
Crest 3D White Brilliance Vibrant Peppermint	Procter & Gamble Cincinnati, OH	72.2	-2.1	0.0
Crest ProHealth Advanced Deep Clean Mint	Procter & Gamble Cincinnati, OH	45.3	-31.4	-14.2

Colgate Max Fresh with Whitening Breath Strips Cool Mint	Colgate-Palmolive New York, NY	35.2	-29.6	-23.7
Crest Complete plus Scope Outlast Ultra	Procter & Gamble Cincinnati, OH	60.0	-32.1	4.9
Listerine Essential Care Original Gel	Johnson & Johnson Consumer Inc. Skillman, NJ	38.2	-34.6	-12.7
Crest Complete plus Scope + Whitening Minty Fresh Liquid Gel	Procter & Gamble Cincinnati, OH	55.9	-37.6	13.3
USP SnF_2	US Pharmacopeia North Bethesda, MD	34.3	-29.6	10.0

Total Iron Content in Toothpaste Samples

Total iron content was determined in a selection of toothpaste samples representative of a broad range of commercially available toothpastes, which are described in TABLES 13A and 13B. Commercial samples were purchased then analyzed for total iron content by a digestion method. An aliquot of 0.25 g was weighed into 15 mL TFM vial (Milestone, Shelton, CT, USA). To each vial, 1 mL of deionized, 18.2 MΩ water, 2.5 mL of nitric acid (67-70% Nitric Acid trace metals basis, VWR International, Radnor, PA, USA), and 1 mL of tetrafluoroboric acid (made in-house from Boric Acid Suprapur >99.9999%, EMD Millipore, Burlington, MA, USA and 47-51% Hydrofluoric Acid Ultra-Trace Metal, VWR International, Radnor, PA, USA) were added. Samples were digested using ultraWAVE microwave digestion system (Milestone, Shelton, CT, USA) using the following program: 25 min ramp to 250 °C, 20 min hold at 250 °C. After digestion, samples were diluted to 50 mL with DI water in polypropylene tubes with addition of yttrium (Y) internal standard. Resulting solutions were taken for ICP-OES analysis (Agilent 5110, Santa Clara, CA, USA). Prepared standards and test solutions were analyzed using three iron wavelengths (Fe 238.204 nm, Fe 234.350 nm, and Fe 259.940 nm) and alternate internal standard (IS) wavelengths to demonstrate selectivity in axial viewing mode. There was an excellent agreement between all three wavelengths. Calibration curves had correlation coefficients, r, equal to 1.00000. Samples were measured in duplicate and the mean sample values were reported. Iron content was back-calculated and reported as μg/g of Fe in the toothpaste.

TABLE 13A. Oral Care Compositions

Crest 3D White Brilliance	Crest 3D White Radiant Mint	Crest ProHealth Sensitive and Enamel Shield	Crest ProHealth Advanced Gum Protection
Glycerin	Water	Water	Glycerin
Hydrated Silica	Sorbitol	Sorbitol	Hydrated Silica
Sodium Hexametaphosphate	Hydrated Silica	Hydrated Silica	Propylene Glycol
Water	Disodium Pyrophosphate	Sodium Lauryl Sulfate	PEG-6
PEG-6	Sodium Lauryl Sulfate	Sodium Gluconate	Water
Flavor	Flavor	Carrageenan	Zinc Lactate
Sodium Lauryl Sulfate	Sodium Hydroxide	Flavor	Flavor
Cocamidopropyl Betaine	Cellulose Gum	Sodium Citrate	Sodium Lauryl Sulfate
Trisodium Phosphate	Sodium Saccharin	Xanthan Gum	Sodium Gluconate
Sodium Saccharin	Carbomer	Zinc Citrate	Sodium Saccharin
PVP	Polysorbate 80	Sodium Hydroxide	Trisodium Phosphate
Carrageenan	Mica	Stannous Chloride	Xanthan Gum
Xanthan Gum	Titanium Dioxide	Sodium Saccharin	PVP
Sucralose	Blue Dye	Sucralose	Carrageenan
Mica	Sodium Fluoride	Titanium Dioxide	Cocamidopropyl Betaine
Titanium Dioxide		Blue Dye	Blue Dye
Sodium Fluoride		Stannous Fluoride	Stannous Fluoride

TABLE 13B. Oral Care Compositions

Crest Tartar Control	Elmex Anti-Caries Professional	Colgate Total SF Clean Mint
Sorbitol	Calcium Carbonate	Water
Water	Water	Sorbitol
Hydrated Silica	Glycerin	Hydrated Silica
Disodium Pyrophosphate	Xylitol	Glycerin
Sodium Lauryl Sulfate	Sodium Lauryl Sulfate	PEG-12
Sodium Hydroxide	Arginine	Tetrasodium Pyrophosphate
Flavor	Flavor	Sodium Lauryl Sulfate
Xanthan Gum	Cellulose Gum	Microcrystalline Cellulose
Sodium Saccharin	Sodium Bicarbonate	Sodium Citrate
Cellulose Gum	Tetrasodium Pyrophosphate	Zinc Phosphate
Carbomer	Benzyl Alcohol	Flavor
Titanium Dioxide	Sodium Saccharin	Cellulose Gum
Blue Dye	Sodium Hydroxide	Sodium Saccharin
Sodium Fluoride	Sodium Monofluorophosphate	Cocamidopropyl Betaine
		Propylene Glycol
		Xanthan Gum
		Citric Acid
		Sucralose
		Titanium Dioxide
		Stannous Fluoride

The results in TABLE 14 indicate that there is a range of possible residual iron content in commercial dentifrices. The tested compositions ranged from at least about 35 μg/g of Fe in Crest Tartar Protection up to about 100 μg/g of Fe in Crest 3D White Brilliance and Crest 3D White Radiant Mint. The pH values of the commercial dentifrices are also given ranging from greater than 5.5 up to about 9.5.

TABLE 14. Total Iron Content

Toothpaste	Total Iron Content (μg/g)	Slurry pH (1g toothpaste:3g water)
Crest Cavity Protection	36.2	7.2
Crest 3D White Brilliance	98.7	7.0
Crest 3D White Radiant Mint	98.7	7.8
Crest ProHealth Sensitive and Enamel Shield	45.1	6.6
Crest ProHealth Advanced Gum Protection	54.4	5.9
Crest Tartar Control	35.6	7.9
Elmex Anti-Caries Professional	37.7	9.3
Colgate Total SF Clean Mint	57.9	7.3

Without wishing to be bound by theory, it is believed that at least about 1, 10, or 30 μg/g of Fe is needed in the absence of stabilizers to cause a color change. Furthermore, it is also believed that stabilizers can prevent the color change in the presence of up to about 100, 250, 500, or 1,000 μg/g of Fe residual total iron in a toothpaste.

The dimensions and values disclosed herein are not to be understood as being strictly limited to the exact numerical values recited. Instead, unless otherwise specified, each such dimension is intended to mean both the recited value and a functionally equivalent range surrounding that value. For example, a dimension disclosed as "40 mm" is intended to mean "about 40 mm."

Every document cited herein, including any cross referenced or related patent or application and any patent application or patent to which this application claims priority or benefit thereof, is hereby incorporated herein by reference in its entirety unless expressly excluded or otherwise limited. The citation of any document is not an admission that it is prior art with respect to any invention disclosed or claimed herein or that it alone, or in any combination with any other reference or references, teaches, suggests or discloses any such invention. Further, to the extent that any meaning or definition of a term in this document conflicts with any meaning or definition of the same term in a document incorporated by reference, the meaning or definition assigned to that term in this document shall govern.

While particular embodiments of the present invention have been illustrated and described, it would be obvious to those skilled in the art that various other changes and modifications can be

made without departing from the spirit and scope of the invention. It is therefore intended to cover in the appended claims all such changes and modifications that are within the scope of this invention.

CLAIMS

What is claimed is:

1. An oral care composition comprising:

hops acid, wherein the hops acid comprises hops alpha acid, hops beta acid, or a combination thereof;

about 1 to about 1,000 μg per gram of the oral care composition of residual iron; and

a stabilization system comprising an iron metal ion chelate, wherein the iron metal ion chelate comprises a polydentate polyphosphate having at least two functional groups, a polycarboxylate having at least three carboxylate groups, or a combination thereof.

2. The oral care composition of claim 1, wherein the iron metal ion chelate has an affinity for ferrous (II) or ferric (III) iron ions, preferably wherein the iron metal ion chelate is an iron (II) metal ion chelate having a log K1 greater than about 2 or is an iron (III) metal ion chelate having a log K1 greater than about 10.

3. The oral care composition of claim 1 or 2, wherein the composition has an improved color stability compared to the composition without the stabilization system.

4. The oral care composition of any one of claims 1-3, wherein the composition is free of a stannous ion source.

5. The oral care composition of any one of claims 1-3, further comprising a stannous ion source.

6. The oral care composition of any one of the preceding claims, further comprising from about 0.01% to about 10%, by weight of the composition, of a metal ion source, preferably wherein the metal ion source comprises a zinc ion source.

7. The oral care composition of any one of the preceding claims, wherein the iron metal ion chelate comprises the polydentate polyphosphate, and the polydentate polyphosphate comprises pyrophosphate or phytate.

8. The oral care composition of any one of the preceding claims, wherein the iron metal ion chelate comprises the polycarboxylate, and the polycarboxylate comprises citrate, preferably wherein the citrate comprises zinc citrate, sodium citrate, or a combination thereof.

9. The oral care composition of any one of the three preceding claims, wherein the stabilization system further comprises gluconate.

10. The oral care composition of any one of the preceding claims, further comprising an abrasive comprising a silica abrasive or a calcium abrasive, preferably wherein the abrasive comprises the calcium abrasive, more preferably wherein the calcium abrasive comprises calcium carbonate.

11. The oral care composition of any one of the preceding claims, wherein:
the oral care composition is essentially free of, substantially free of, or free of silica;
the oral care composition is essentially free of, substantially free of, or free of fluoride; or
a combination thereof.

12. The oral care composition of any one of claims 1-10, further comprising a fluoride ion source.

13. The oral care composition of any one of the preceding claims, wherein the hops acid comprises only non-hydrogenated hops acid.

14. The oral care composition of any one of the preceding claims, wherein the oral care composition comprises from about 0.05% to about 10%, preferably from about 0.05% to about 5%, or more preferably from about 0.05% to about 2%, by weight of the composition, of the hops beta acid or wherein the oral care composition comprises from about 0.05% to about 10%, preferably from about 0.05% to about 5%, or more preferably from about 0.05% to about 2%, by weight of the composition, of the hops alpha acid.

15. The oral care composition of any one of the preceding claims, wherein the oral care composition comprises from about 0.1% to about 10%, preferably from about 0.1% to about 5%, or more preferably from about 1% to about 4%, by weight of the composition, of the stabilization system.

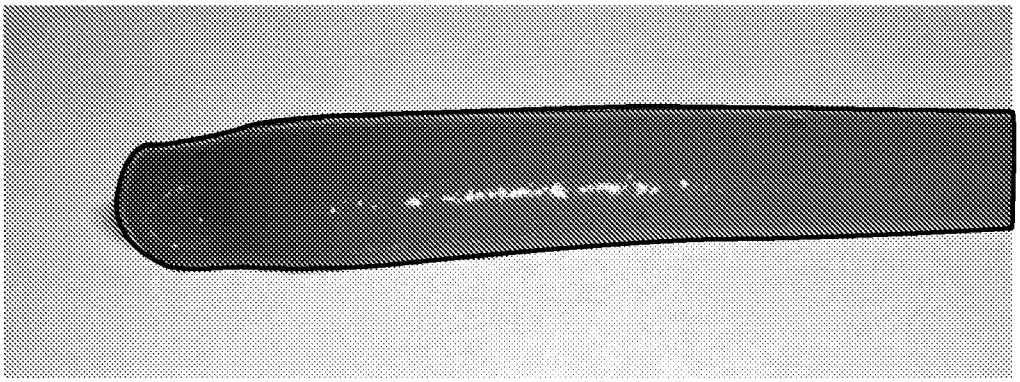


FIG. 1A

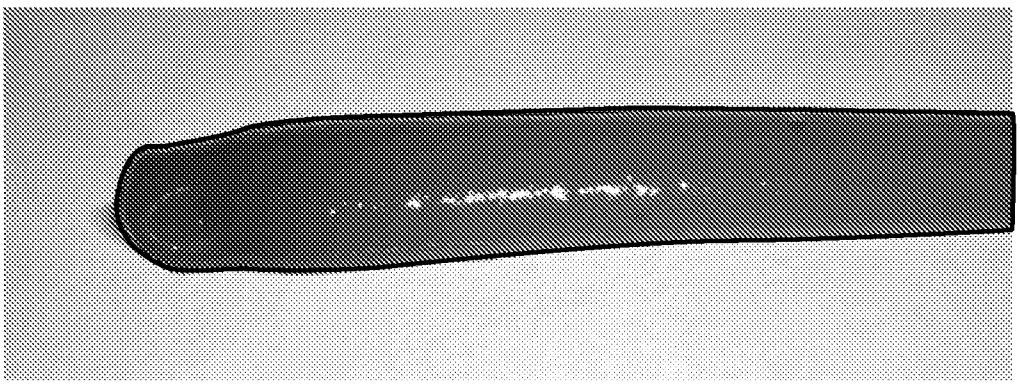
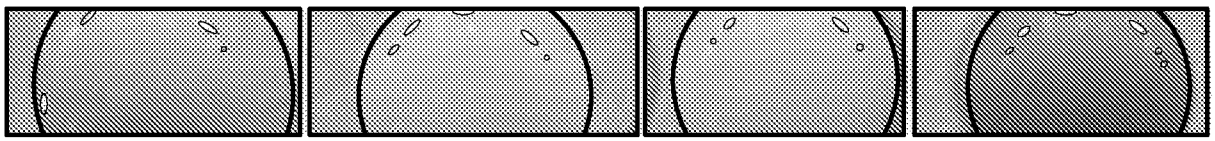
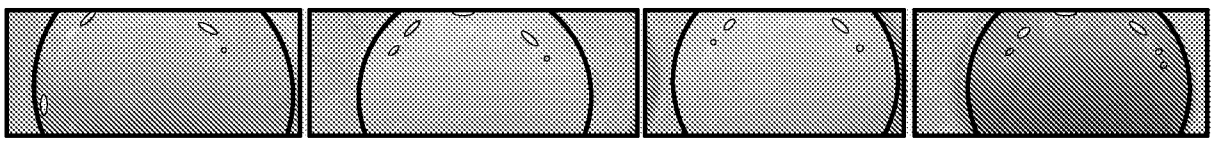


FIG. 1B



Ex. 2A Ex. 2B Ex. 2C Ex. 2D

FIG. 2A



Ex. 2A Ex. 2B Ex. 2C Ex. 2D

FIG. 2B

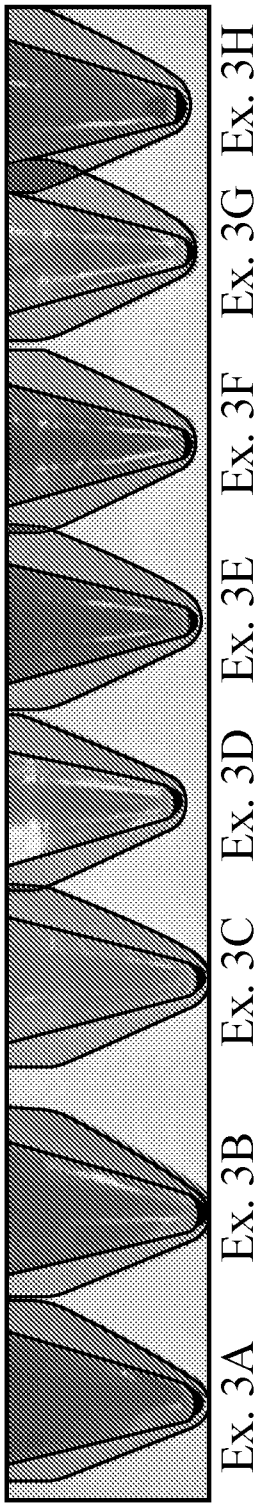

Ex. 3A
Ex. 3B
Ex. 3C
Ex. 3D
Ex. 3E
Ex. 3F
Ex. 3G
Ex. 3H

FIG. 3A

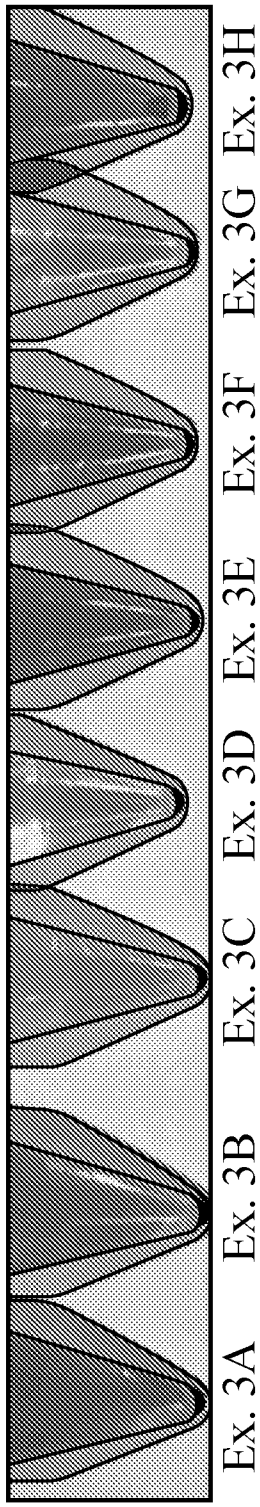

Ex. 3A
Ex. 3B
Ex. 3C
Ex. 3D
Ex. 3E
Ex. 3F
Ex. 3G
Ex. 3H

FIG. 3B

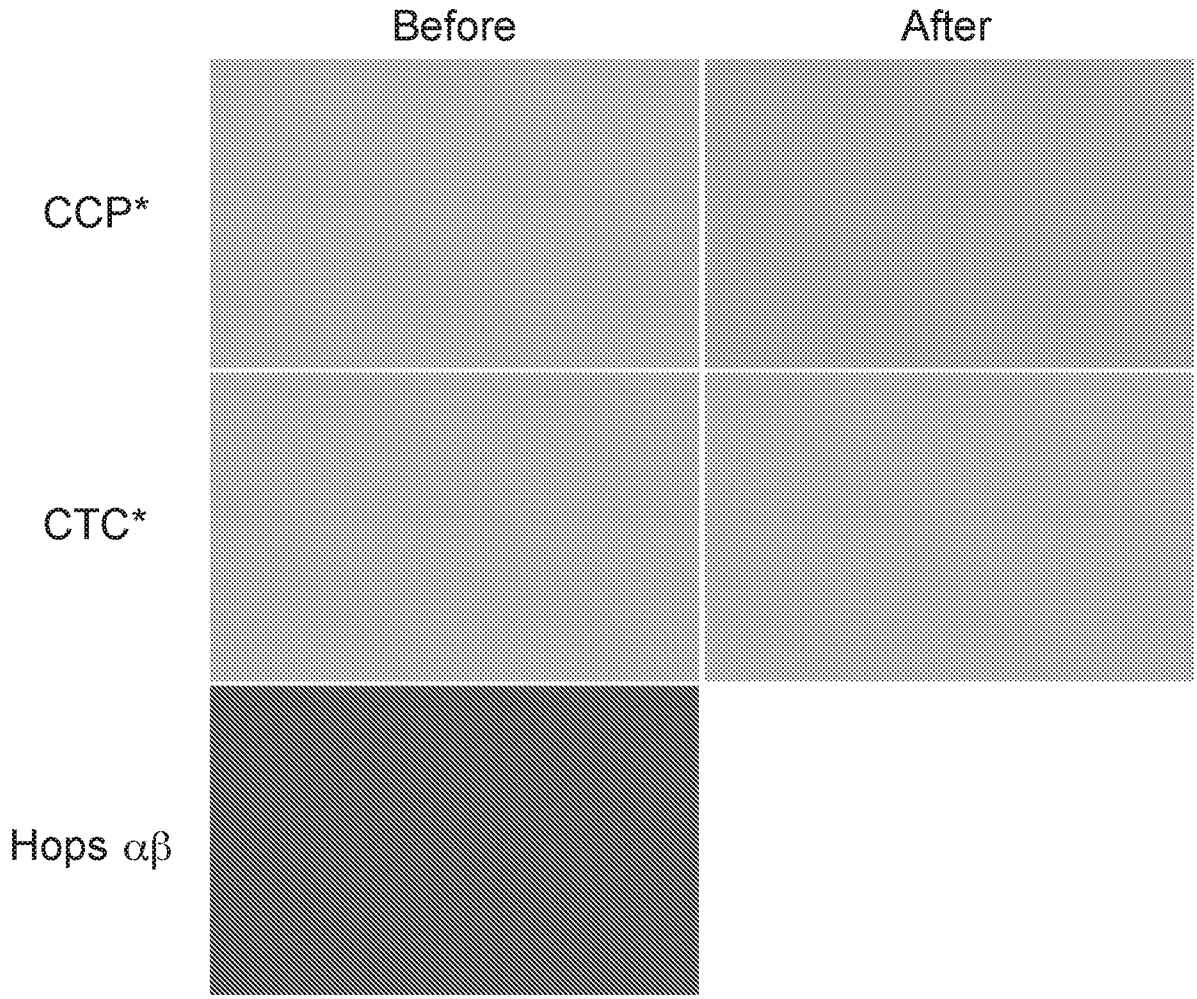


FIG. 4

INTERNATIONAL SEARCH REPORT

International application No
PCT/CN2024/101836

ECT MATTER
INV. A61K8/19 A61K8/24 A61K8/365 A61K8/55 A61K8/9789
A61Q11/00
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)
A61K A61Q

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)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2021/063378 A1 (PROCTER & GAMBLE [US]; SHI YUNMING [CN] ET AL.) 8 April 2021 (2021-04-08)	1-3,5,6, 9-11, 13-15
Y	claim 1 examples 2-4; table 1	1-15

X	US 2022/096363 A1 (BAIG ARIF ALI [US] ET AL) 31 March 2022 (2022-03-31)	1-4,10, 12-15
Y	claim 1 formulas A-J; tables 3a, 3b, 5	1-15

X	US 2022/096341 A1 (BAIG ARIF ALI [US] ET AL) 31 March 2022 (2022-03-31)	1-3,5,6, 8-10, 12-15
Y	claims 1-7 examples 2C, 3B, 3D and 4D; tables 4-7	1-15

	-/--	

[X] Further documents are listed in the continuation of Box C.

[X] 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

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"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	Date of mailing of the international search report
18 September 2024	30/09/2024

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, Fax: (+31-70) 340-3016	Briand, Benoit

2

Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No
PCT/CN2024/101836

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2006/134024 A1 (TRIVEDI HARSH M [US] ET AL) 22 June 2006 (2006-06-22)	1-4,6,7, 10,12-15
Y	claim 1; table 1	1-15

2

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/CN2024/101836

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2021063378 A1	08-04-2021	AU 2020359944 A1	10-03-2022
		BR 112022004397 A2	14-06-2022
		CA 3155883 A1	08-04-2021
		CN 114466680 A	10-05-2022
		EP 4037765 A1	10-08-2022
		JP 7386335 B2	24-11-2023
		JP 2022549843 A	29-11-2022
		US 2021121392 A1	29-04-2021
		US 2024156715 A1	16-05-2024
		WO 2021062607 A1	08-04-2021
		WO 2021063378 A1	08-04-2021
US 2022096363 A1	31-03-2022	AU 2021350111 A1	16-03-2023
		BR 112023002550 A2	04-04-2023
		CA 3190969 A1	31-03-2022
		CN 116710059 A	05-09-2023
		EP 4216915 A1	02-08-2023
		JP 2023542022 A	04-10-2023
		US 2022096363 A1	31-03-2022
		WO 2022067142 A1	31-03-2022
US 2022096341 A1	31-03-2022	AU 2021350837 A1	16-03-2023
		BR 112023002883 A2	04-04-2023
		CA 3190974 A1	31-03-2022
		CN 116209418 A	02-06-2023
		EP 4216908 A1	02-08-2023
		JP 2023542025 A	04-10-2023
		US 2022096341 A1	31-03-2022
		WO 2022067140 A1	31-03-2022
US 2006134024 A1	22-06-2006	AR 052839 A1	04-04-2007
		AT E443511 T1	15-10-2009
		AU 2005319183 A1	29-06-2006
		BR PI0519635 A2	03-03-2009
		CA 2592123 A1	29-06-2006
		CN 101123943 A	13-02-2008
		CN 103893071 A	02-07-2014
		DK 1827363 T3	11-01-2010
		EP 1827363 A1	05-09-2007
		ES 2333809 T3	01-03-2010
		HK 1107023 A1	28-03-2008
		PL 1827363 T3	26-02-2010
		TW 200637607 A	01-11-2006
		US 2006134024 A1	22-06-2006
		WO 2006069209 A1	29-06-2006
		ZA 200706045 B	31-12-2008