

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
6 July 2006 (06.07.2006)

PCT

(10) International Publication Number
WO 2006/071655 A1

(51) International Patent Classification:
A61K 8/97 (2006.01) *A61Q 11/00* (2006.01)

(21) International Application Number:
PCT/US2005/046242

(22) International Filing Date:
21 December 2005 (21.12.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/639,079 23 December 2004 (23.12.2004) US
60/639,080 23 December 2004 (23.12.2004) US
11/256,860 24 October 2005 (24.10.2005) US

(71) Applicant (*for all designated States except US*): **COLGATE-PALMOLIVE COMPANY** [US/US]; 300 Park Avenue, New York, New York 10022 (US).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **WORRELL, Cortney, L.** [US/US]; 253 Greenbrook Road North, Plainfield, New Jersey 07060 (US). **TRIVEDI, Harsh, M.** [US/US]; 134 Grantham Drive, Somerset, New Jersey 08873 (US). **PANALIGAN, Kimberlee** [US/US]; 23 Frederick Place, Parlin, New Jersey 08859 (US). **XU, Tao** [US/US]; 41 Jernee Drive, East Brunswick, New Jersey 08816 (US).

(74) Agent: **BULLOCK, Kristyne, A.**; Colgate-Palmolive Company, 909 River Road, Piscataway, New Jersey 08855 (US).

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

(84) Designated States (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- *with international search report*
- *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: ORAL CARE COMPOSITION CONTAINING EXTRACT OF UNOXIDIZED CAMELLIA

(57) Abstract: An oral composition for at least one or treating and inhibiting an oral inflammatory condition comprising: a *Camellia* extract including at least about 30% epigallocatechin gallate, at least about 50% total catechins, and at least about 60% total polyphenols; and a substantially water insoluble non-cationic anti-bacterial agent.



WO 2006/071655 A1

TITLE OF THE INVENTION

Oral Care Composition Containing Extract of Unoxidized *Camellia*

CROSS REFERENCE TO RELATED APPLICATIONS

The application claims priority to United States Provisional Patent Application Serial Nos. 60/639,079 and 60/639,080, each filed on December 23, 2004, the contents of each of which are incorporated herein by reference.

BACKGROUND OF THE INVENTION

[0001] Oral inflammations, such as gingivitis and periodontitis, are common oral conditions. Gingivitis, which is an inflammation of the gums, is the initial stage of gum disease. The direct cause of gingivitis is plaque, which is a soft, sticky, colorless film including bacteria that forms on the teeth and gums. Plaque, if left untreated, produces toxins that can inflame or infect the gum tissue to cause gingivitis. Untreated gingivitis can eventually spread from the gums to the ligaments and bone that support the teeth, thus causing periodontitis. While a variety of different treatments exist for preventing and suppressing oral inflammatory conditions, such treatments are subject to improvement.

[0002] Antioxidants are compounds that help inhibit oxidation reactions caused by active or free radical oxygen. Active oxygen naturally occurs in the body as a result of chemical reactions during normal cellular processes. Active oxygen can also be formed in response to excess pollution, too much UV sunlight, and exposure to cigarette smoke. In an attempt to stabilize, active oxygen molecules bond with other molecules of the body to oxidize them, which leads to, for example, destruction of cell membranes, damage to DNA, and oxidation of lipids (fats). Oxidation can ultimately lead to cancer, heart disease, stroke, rheumatoid arthritis, cataracts, and Alzheimer's disease.

[0003] Antioxidants can inhibit oxidation reactions in a number of different ways. For example, antioxidants can scavenge reactive oxygen free radical species and/or decrease localized oxygen concentration thereby reducing molecular oxygen's oxidation potential. Various antioxidants exist and antioxidants can be derived from a variety of different sources. Exemplary antioxidants include Vitamin E, Vitamin C, carotenoids, and polyphenols, such as flavonoids.

BRIEF SUMMARY OF THE INVENTION

[0004] In an embodiment of the present invention, an oral composition for at least one of treating and inhibiting an oral inflammatory condition is provided. The oral composition comprises: a *Camellia* extract including at least about 30% epigallocatechin gallate, at least about 50% total catechins, and at least about 60% total polyphenols; and a substantially water insoluble non-cationic anti-bacterial agent.

[0005] In another embodiment of the present invention, a method of at least one of treating and inhibiting an oral inflammatory condition is provided. The method comprises administering to an oral cavity of a subject in need thereof an effective amount of an oral composition comprising a *Camellia* extract including at least about 30% epigallocatechin gallate, at least about 50% total catechins, and at least about 60% total polyphenols.

[0006] In yet another embodiment of the present invention, a method of at least one of treating and inhibiting an oral inflammatory condition and providing antioxidant activity in an oral cavity is provided. The method includes administering to an oral cavity of a human or other animal subject in need thereof an effective amount of an oral composition comprising: a *Camellia* extract including at least about 30% epigallocatechin gallate, at least about 50% total catechins, and at least about 60% total polyphenols; and a halogenated diphenyl ether anti-bacterial agent.

[0007] In various embodiments, the compositions and methods of the present invention further comprise an anti-bacterial agent, such as triclosan. In various embodiments, the compositions and methods further comprise a rosemary extract.

[0008] It has been discovered that compositions and methods of this invention afford advantages over anti-inflammatory and antioxidant compositions and methods among those known in the art. Such advantages include the use of an oral composition including a natural green tea extract to provide enhanced anti-inflammatory activity and enhanced anti-oxidant activity. Further uses, benefits, and embodiments of the present invention are apparent from the description set forth herein.

DETAILED DESCRIPTION OF THE INVENTION

[0009] Oral compositions according to the present invention comprise an extract obtained from tissue of a member of the genus *Camellia*. The compositions of the invention may exhibit an anti-inflammatory and/or antioxidant effect when introduced to the oral cavity. This

anti-inflammatory and/or antioxidant activity may be increased when the oral compositions of the invention also include other antibacterial agents, such as triclosan and/or rosemary extract.

[0010] The present invention, in various embodiments, can provide oral compositions for treating and/or inhibiting oral inflammation and for introducing an antioxidant activity to the oral cavity. The oral composition may take any dosage form useful for oral administration. Illustrative examples of these include: a dentifrice, *e.g.*, a toothpaste, dental gel, dental cream, or tooth powder; a mouthwash, mouth rinse, or mouth spray; an oral slurry or liquid dentifrice; a gum or other confectionary; a lozenge; dental floss or dental tape; a prophylaxis paste or powder; a mono- or multi-layer oral film or gel strip, *e.g.*, tooth strips or breath strips, preferably using a biodegradable or orally consumable film or gel; functional film or gel flakes or functional milli-, micro-, or nano-particles; a film-forming composition comprising pre-gel(s) or pre-polymer(s), *e.g.*, film-forming dentifrices, dental paints; a tooth hardener; or a coating on an oral, *e.g.*, orthodontic, appliance or implant.

[0011] The present invention provides oral compositions comprising *Camellia* extract. The *Camellia* extract is obtained from substantially unoxidized plant tissues, of the genus *Camellia*. Any variety, form, or subspecies of genus *Camellia* may be used although extracts of unoxidized *Camellia sinensis* may be preferred. Also preferred may be the subspecies or variants: *C. sinensis* var. *assamica*, *C. assamica* and var. *kucha*; *C. sinensis* var. *cambodiensis*, subsp. *lasiocalyx* and var. *Shan*; *C. sinensis* var. *dehungensis*; *C. sinensis* var. *pubilimba*; and *C. sinensis* var. *sinensis*, *bohea*, *macrophylla*, *parvifolia*, and *waldenae*.

[0012] In a preferred embodiment, the *Camellia* extract may be obtained from the substantially unoxidized tissue(s) of *C. sinensis* var. *assamica*, *C. sinensis* var. *cambodiensis*, or *C. sinensis* var. *sinensis*; in a preferred embodiment, the extract will be made from substantially unoxidized tissue(s) of *C. sinensis* var. *assamica* or *C. sinensis* var. *sinensis*; in a preferred embodiment, the extract may be obtained from a substantially unoxidized tissue(s) of *C. sinensis* var. *sinensis*. Regardless of the source, leaf tissue may be preferred, although any of leaf buds; flowers, flower buds; stems, twigs; stem, twig, and trunk bark; roots; root bark; and other aerial and reproductive parts and combinations of the same may be used.

[0013] The *Camellia* extract may be in any form, including powder, suspension, emulsion and/or an oil.

[0014] *Camellia* tissue(s) used for production of any extract for use in the invention may be prepared by any means known in the art. For example, if using leaves, the leaves should be harvested while still green in color and heated very soon after they have been picked, *e.g.*, before about thirty minutes, more commonly before about ten minutes post-harvest. The heating can be performed by any mechanism: pan-firing, steaming, roasting, microwaving, so long as the temperature is rapidly raised (in about 5-15 minutes or less) to a level at which the catabolic enzymes present in the tissue are substantially denatured. After this heating step, the leaves may be air dried, or otherwise dehydrated.

[0015] The plant tissues processed in the above described way or in any other manner may be extracted using any suitable known extraction technique to provide an extract useful in the present invention. For example, extraction techniques that can be used include any suitable aqueous extraction or organic solvent extraction. Preferred extraction techniques utilize water, methanol, water/methanol, dichloromethane and methanol:THF. Any other suitable extraction technique may be used, such as steam distillation and supercritical fluid extraction.

[0016] The *Camellia* extract may be present in the oral composition in various amounts. Preferably, the *Camellia* extract is present in an amount greater than about 0.001%; preferably from about 0.001% to about 20%; preferably from about 0.01% to about 15%; preferably from about 0.05% to about 10%; preferably from about 0.05% to about 5%; preferably from about 0.05% to about 1%; and preferably from about 0.1% to about 0.2%.

[0017] The invention may also include vitamin (tocopherol) and/or derivatives, or analogs of the same. For example, tocopherols of the present invention include substances that have the biological and physiological activities of Vitamin E, including alpha-, beta-, gamma-, delta-, epsilon-, zeta- and eta-tocopherols of natural d- and synthetic dl-forms; substituted tocopherols in which one, two or three of the methyl groups in the 5, 7 and 8 positions of the chromanol nucleus of tocopherol are replaced by a radical or radicals, such as alkyl, haloalkyl, hydroxyalkyl, aminoalkyl, acyl and allyl radicals, and in which the methyl group in the 2 position of the chromanol nucleus of the tocopherol is replaced by a lower alkyl radical, such as ethyl, propyl and butyl; and tocopherol analogous substances such as nor-tocopherol in which the isoprene units in the 2 position of the chromanol nucleus are two in number, homo-tocopherol in which the isoprene units are four in number and iso-tocopherol in which a side chain composed of three isoprene units in the tocopherol is linear.

[0018] While the oral composition of the present invention can include any suitable natural or synthetic Vitamin E tocopherol, Vitamin E (dl- α tocopherol) (C₂₉H₅₀O₂, mw 430.72) is preferred. Vitamin E is available from various different sources, such as Royal DSM N.V. of The Netherlands. Vitamin E can be present in the oral composition at various different levels. For example, Vitamin E can be present in an effective amount to provide antioxidant efficacy. For example, Vitamin E can be present from about 10 to about 10,000 ppm, from about 15 to about 40 ppm, from about 20 to 30 ppm, or about 25 ppm. Also, Vitamin E can be present in the oral composition greater than about 0.001%, from about 0.001% to about 5%, from about 0.01% to about 5%, from about 0.2% to about 4%, and from about 0.3% to about 3%.

[0019] The oral composition of the invention may include one or more additional therapeutic agents, such as anti-bacterial agents or anti-inflammatory agents. Exemplary antibacterial agents may include halogenated diphenyl ethers, benzoic esters, halogenated carbanilides, 8-hydroxyquinoline and salts thereof; zinc and stannous ion sources such as zinc citrate, zinc sulphate, zinc glycinate, sodium zinc citrate and stannous pyrophosphate; copper (II) compounds such as copper (II) chloride, fluoride, sulfate and hydroxide; phthalic acid and salts thereof such as magnesium monopotassium phthalate; sanguinarine; quaternary ammonium compounds, such as alkylpyridinium chlorides (*e.g.*, cetylpyridinium chloride (CPC), combinations of CPC with zinc and/or enzymes, tetradecylpyridinium chloride, and N-tetradecyl-4-ethylpyridinium chloride); bisguanides, such as chlorhexidine digluconate, hexetidine, octenidine, and alexidine; halogenated bisphenolic compounds, such as 2,2'-methylenebis-(4-chloro-6-bromophenol); benzalkonium chloride; salicylanilide, halogenated salicylanilides; domiphen bromide; iodine; sulfonamides; bisbiguanides; phenolic compounds such as phenol and its homologs, mono- and poly-alkyl and aralkyl halophenols, and bisphenolic compounds; piperidino derivatives such as delmopinol and octapinol; magnolia extract; grapeseed extract; thymol; eugenol; menthol; geraniol; carvacrol; citral; eucalyptol; catechol; 4-allylcatechol; resorcinol and its derivatives, such as hexyl resorcinol; methyl salicylate; antibiotics such as augmentin, amoxicillin, tetracycline, doxycycline, minocycline, metronidazole, neomycin, kanamycin and clindamycin; and mixtures thereof. A further illustrative list of agents is provided in U.S. Patent Nos. 5,776,435; 5,681,548; 5,912,271 and 5,723,500, then contents of each of which are incorporated herein by reference.

[0020] The oral composition can, and preferably will, also include one or more solubilizing agents to solubilize the *Camellia* extract. The solubilizing agent can be any solubilizing agent that is effective to solubilize *Camellia* extract. For example, in various embodiments the solubilizing agent can be at least one of an orally acceptable surfactant, flavoring oil, alcohol, and solubilizing humectant (*e.g.*, propylene glycol).

[0021] Examples of surfactants that can be used include anionic, nonionic, amphoteric, zwitterionic, and cationic synthetic detergents. Anionic surfactants include the water-soluble salts of alkyl sulfates having 8-20 carbon atoms in the alkyl radical (such as sodium alkyl sulfate), a monoalkyl phosphate compound having 6-18 carbon atoms, the water-soluble salts of sulfonated monoglycerides of fatty acids having from 8-20 carbon atoms (such as sodium lauryl sulfate (>82% pure) and sodium coconut monoglyceride sulfonates), an alkyl glycoside that is mono[alkyl(C₁₂-C₂₂)] – [(Glyc)1-20], sarcosinates (such as sodium and potassium salts of lauroyl sarcosinate, myristoyl sarcosinate, palmitoyl sarcosinate, stearyl sarcosinate and oleoyl sarcosinate), taurates, higher alkyl sulfoacetates (such as sodium lauryl sulfoacetate), isothionates (such as sodium lauroyl isothionate), sodium laureth carboxylate, sodium dodecyl benzenesulfonate, and mixtures of the foregoing. Preferred are the sarcosinates since they inhibit acid formation in the mouth due to carbohydrate breakdown. Nonionic surfactants include poloxamers; polyoxyethylene sorbitan esters; fatty alcohol ethoxylates; polyethylene oxide condensates of alkyl phenols; products derived from the condensation of ethylene oxide with fatty acids, fatty alcohols, fatty amides, or polyhydric alcohols; and polypropyleneoxide or ethylene oxide condensates of aliphatic alcohols; long-chain tertiary amine oxides; long-chain tertiary phosphine oxides; long-chain dialkyl sulfoxides; and mixtures of such materials. Amphoteric surfactants include betaines (such as cocamidopropylbetaine), derivatives of aliphatic secondary and tertiary amines in which the aliphatic radical can be a straight or branched chain and wherein one of the aliphatic substituents contains about 8-18 carbon atoms and one contains an anionic water-solubilizing group (such as carboxylate, sulfonate, sulfate, phosphate or phosphonate), and mixtures of such materials. Zwitterionic surfactants include derivatives of aliphatic quaternary ammonium, phosphonium and sulfonium compounds in which the aliphatic radical can be a straight or branched chain and wherein one of the aliphatic substituents contains about 8-18 carbon atoms and one contains an anionic water-solubilizing group (such as carboxy, sulfonate, sulfate, phosphate or phosphonate). Cationic

surfactants include aliphatic quaternary ammonium compounds having one long alkyl chain containing about 8-18 carbon atoms (such as lauryl trimethylammonium chloride, cetylpyridinium chloride, cetyltrimethylammonium bromide, diisobutylphenoxyethyldimethylbenzylammonium chloride, coconut alkyltrimethylammonium nitrite, cetylpyridinium fluoride). Certain cationic surfactants can also act as antimicrobials.

[0022] The solubilizing agent(s) are preferably present at about 0.02% to about 50% by weight of the composition.

[0023] The oral composition can also optionally include an enhancing agent (EA) that is a water soluble or swellable anionic polymer or co-polymer comprising delivery enhancing groups and retention enhancing groups. The delivery enhancing groups enhance delivery of the *Camellia* extract to teeth and oral tissue. The retention enhancing groups enhance retention by the teeth and the oral tissue of the *Camellia* extract. The enhancing agents of the present invention can include those that are characterized as having utility as denture adhesives or fixatives or dental cements. The enhancing agent is a polymer or copolymer, which terms are entirely generic, thus including for example oligomers, homopolymers, copolymers of two or more monomers, ionomers, block copolymers, graft copolymers, cross-linked polymers and copolymers, and the like. The EA may be natural or synthetic, and water (saliva) soluble or swellable (hydratable, hydrogel forming) polymer or copolymer. The EA can be selected to have various sizes, such as an (weight) average molecular weight (MW) of: about 100 to about 1,000,000; about 1,000 to about 1,000,000; or about 2,000 to about 2,500, or from about 250,000 to about 500,000. Also, the delivery enhancing groups of the EA can be any of those listed in U.S. Patent Nos. 5,538,715 and 5,776,435, the contents of each of which are incorporated by reference.

[0024] The delivery-enhancing group refers to one that attaches or substantively, adhesively, cohesively or otherwise bonds the EA, carrying components of the *Camellia* extract to oral (e.g. tooth and gum) surfaces, thereby "delivering" the components to such surfaces. The organic retention-enhancing group, which is generally hydrophobic, attaches or otherwise bonds the *Camellia* extract to the EA, thereby promoting retention of the *Camellia* extract directly on the EA and indirectly on the oral surface(s). In some instances, attachment of the *Camellia* extract may alternatively or additionally occur through physical entrapment thereof by the EA, especially when the EA is a cross-linked polymer, the structure of which inherently provides

increased sites for such entrapment. The presence of a higher molecular weight, more hydrophobic cross-linking moiety in the cross-linked polymer still further promotes the physical entrapment of the *Camellia* extract in or on the cross-linked EA polymer.

[0025] The oral compositions comprise an orally acceptable vehicle. Any suitable orally acceptable vehicle can be used, such as those described in U.S. Patent No. 4,894,220 titled "Antibacterial Anti-Plaque Oral Composition," which is incorporated by reference herein. For example, the vehicle can include a water-phase with humectant. In the present invention, the water and humectant liquid phase can comprise at least about 10% by weight of the oral composition. Moreover, preferably the humectant comprises propylene glycol, which can help to solubilize the *Camellia* extract. The remainder of the humectant is preferably glycerine and/or sorbitol and/or xylitol. Water is present typically in amount of at least about 3% by weight; and glycerine and/or sorbitol and/or xylitol typically total about 6.5% to about 75% by weight of the oral preparation, more typically about 10% to about 75%, and, together with the solubilizing humectant, the essential humectant components typically amount to about 7% to about 80% by weight of the oral preparation. Reference hereto to sorbitol refers to the material typically as available commercially in about 70% aqueous solutions. Where the composition contains a substantially water insoluble noncationic anti-bacterial agent, the composition will preferably be free of at least significant amounts of polyethylene glycol, particularly of average molecular weight of about 600 or more, since polyethylene glycol can inhibit the antibacterial activity of a noncationic antibacterial agent, even when another component, such as, propylene glycol is present to effect its solubilization.

[0026] The vehicle can also be a water-alcohol mixture. Generally, the weight ratio of water to alcohol is in the range of from about 1:1 to about 20:1, preferably about 3:1 to about 10:1 and more preferably about 4:1 to about 6:1. The total amount of water-alcohol mixture in, for example, a mouthwash is typically in the range of from about 70 to about 99.9% by weight. The alcohol is a non-toxic alcohol such as ethanol or isopropanol. A humectant, such as glycerine, sorbitol, or xylitol may be present in an amount of about 10 to about 30% by weight. The oral composition may contain water at about 5% to about 30% by weight. Liquid dentifrices typically contain about 50% to about 85% of water, may contain about 0.5% to about 20% by weight of non-toxic alcohol and may also contain about 10% to about 40% by weight of humectant, such as glycerine, sorbitol, and/or xylitol. Sorbitol refers to the material typically

available commercially in about 70% aqueous solutions. Ethanol is the preferred non-toxic alcohol. The alcohol assists in dissolving the *Camellia* extract and the water-insoluble non-cationic anti-bacterial agent.

[0027] It may be desirable to include within the dentifrice composition one or more therapeutic agents that prevent, treat and/or reduce the symptoms related to various oral or systemic diseases or conditions. Useful therapeutic agents include all those known or developed in the art including steroids, NSAIDs, a fluoride ion source, polycarboxylate polymers, polyvinyl methyl ether/maleic anhydride (PVME/MA) copolymers, an arginine ester, a zinc ion source, a stannous ion source, delmopinol, tartar control agents, an antibacterial agent, triclosan and salts thereof, chlorhexidine, alexidine, hexetidine, sanguinarine, benzalkonium chloride, salicylanilide, domiphen bromide, cetylpyridinium chloride (CPC), tetradecylpyridinium chloride (TPC), N-tetradecyl-4-ethylpyridinium chloride (TDEPC), octenidine, octapinol, nisin, a zinc ion source, a copper ion source, an essential oil, a furanone, anti-inflammatory agents, antiplaque agents, antioxidants, and bacteriocins, and salts thereof, honokiol, vitamins, anti-attachment agents, proteinaceous agents, peptides. A further illustrative list of useful antibacterial agents is provided in U.S. Patent 5,776,435, the contents of which are incorporated herein by reference.

[0028] Abrasives may be added to the dentifrice formulation if desired. Any suitable oral care abrasive or polishing agent may be used. Preferred may be silica abrasives such as precipitated silicas, sodium metaphosphate, potassium metaphosphate, tricalcium phosphate, dihydrated dicalcium phosphate, aluminum silicate, calcined alumina, bentonite or other siliceous materials, particulate thermosetting resins, such as melamine, phenolic, and urea-formaldehydes, and cross-linked polyepoxides and polyesters.

[0029] As desired, any other additives may be included in the dentifrice composition for reasons of *e.g.*, manufacturing, stability, aesthetics, therapeutic effect, consumer appeal, etc. Exemplary additives include all other conventional dentifrice additives, viscosity modifiers, diluents, foam modulators, saliva stimulating agents, desensitizing agents, whitening agents, enzymes, pH modifying agents, mouth-feel agents, sweeteners, colorants, opacifiers, and breath freshening agents.

[0030] The present invention provides for methods and processes of using the oral compositions of the present invention to treat and inhibit oral conditions, such as oral

inflammatory conditions, dental plaque deposits on the teeth and oral tissues, and dental calculus. Further, the oral compositions can serve as antioxidants. The present invention provides for commercial packaging for the oral compositions to distribute and store the oral compositions.

[0031] The oral compositions can be applied to the subject in any suitable manner, as is known in the art. For example, the oral compositions can be applied to the subject's oral cavity using a suitable applicator or delivery device, such as a brush, dental strip, film, syringe, tape, gum, pill, or any other applicator or delivery device that is known in the art. The compositions can be used in prophylactic methods and processes to promote and maintain oral health, appearance, and breath freshness. The oral compositions can be repeatedly applied to the subject over a number of days according to a particular treatment schedule to treat and/or inhibit dental plaque deposits, dental calculus deposits, and oral inflammatory conditions and to provide anti-oxidant activity. Instructions setting forth the treatment schedule can be provided with the commercial packaging.

[0032] The present invention is further illustrated through the following non-limiting examples.

Example 1

[0033] A powder and/or oil extract is obtained from *Camellia sinensis*. The extract is commercially available from, for example, Sabinsa, Corp. and can be Sabinsa specification no. MS-0726-01. The *Camellia* extract can include at least about 30% epigallocatechin gallate, at least about 50% total catechins, and at least about 60% total polyphenols. The extract is introduced to an *in vitro* cell culture assay system of human embryonic palatal mesenchyme cells stimulated with IL1 β . Prostaglandin E2 (PGE2) production is measurably inhibited when the extract is introduced to the assay. PGE2 is known to cause inflammation. Therefore, use of the extract to inhibit PGE2 production advantageously reduces and inhibits inflammation.

Example 2

[0034] Solution containing the anti-inflammatory Triclosan and the *Camellia* extract is prepared. The *Camellia* extract is present at a concentration below that required for the *Camellia* extract to act as an anti-inflammatory agent alone. The solution exhibits increased anti-inflammatory activity as compared to solutions of Triclosan alone. Therefore, *Camellia* extract advantageously acts synergistically with Triclosan to enhance the anti-inflammatory effect of Triclosan.

Example 3

[0035] The *Camellia* extract is included in an oral care product at various concentrations, such as a dentifrice at about 0.01%, about 10%, or any concentration between about 0.01% and about 10%, along with one or more suitable surfactants. The oral care product may also include concentrations of Triclosan and/or rosemary extract.

Example 4

[0036] The *Camellia* extract is included in an oral care product at various concentrations, such as an oral care portable strip at 0.1%, 0.2%, or any concentration between 0.1% and 0.2%, along with one or more suitable surfactants. The oral care strip is introduced into an in vitro system containing lipid peroxides undergoing oxidation. The oral care strip advantageously reduces the oxidation of lipid peroxides *in vitro* to provide antioxidant activity.

[0037] The examples and other embodiments described herein are exemplary and not intended to be limiting in describing the full scope of compositions and methods of this invention. Equivalent changes, modifications and variations of specific embodiments, materials, compositions and methods may be made within the scope of the present invention, with substantially similar results.

CLAIMS

We claim:

1. An oral composition for the treatment, inhibition or reduction of an oral inflammatory condition comprising:
a *Camellia* extract including at least about 30% epigallocatechin gallate, at least about 50% total catechins, and at least about 60% total polyphenols; and
a substantially water insoluble non-cationic anti-bacterial agent.
2. An oral composition according to claim 1 further comprising more than about 0.001% by weight of Vitamin E.
3. The composition according to claim 1, wherein the Vitamin E is dl- α tocopherol.
4. The composition according to claim 1, wherein the Vitamin E is present in the composition in an amount of about 0.001% to about 5% by weight.
5. The composition according to claim 1, wherein the Vitamin E is present in the composition in an amount of about 0.1% to about 4% by weight.
6. The composition according to claim 1, wherein the Vitamin E is present in the oral composition in an amount of about 0.2% to about 2.5% by weight.
7. A composition according to claim 1, wherein the *Camellia* extract is an extract of *Camellia sinensis* tissue.
8. A composition according to claim 1, wherein the *Camellia* extract is obtained from tissue of at least one of *Camellia sinensis* var. *assamica*, *Camellia sinensis* var. *cambodiensis*, *Camellia sinensis* var. *dehungensis*, *Camellia sinensis* var. *pubilimba*, and *Camellia sinensis* var. *sinensis*.

9. A composition according to claim 1, wherein the *Camellia* extract is present in the oral composition about 0.001% to about 20% by weight.

10. A composition according to claim 1, wherein the *Camellia* extract is present in the oral composition about 0.01% to about 10% by weight.

11. A composition according to claim 1, wherein the *Camellia* extract is present in the oral composition about 0.01% to about 5% by weight.

12. A composition according to claim 1, wherein the *Camellia* extract is present in the oral composition about 0.1% to about 0.2% by weight.

13. A composition according to claim 1, wherein the *Camellia* extract is present in the oral composition in an amount that is less than the minimum amount of the *Camellia* extract that exhibits anti-inflammatory activity when the *Camellia* extract is present as the sole component therein having anti-inflammatory activity.

14. A composition according to claim 1, wherein the anti-bacterial agent is a halogenated diphenyl ether.

15. A composition according to claim 14, wherein the anti-bacterial agent is 2',4,4'-trichloro-2-hydroxy-diphenyl ether.

16. A composition according to claim 1, wherein the oral composition comprises at least one botanical extract selected from the group consisting of magnolia extracts, rosemary extracts, and mixtures thereof.

17. A composition according to claim 16, wherein the botanical extract is rosemary extract.

18. A method of at least one of treating and inhibiting an oral inflammatory condition comprising administering to an oral cavity of a subject in need thereof an effective amount of an oral composition comprising a *Camellia* extract including at least about 30% epigallocatechin gallate, at least about 50% total catechins, and at least about 60% total polyphenols.

19. A method according to claim 18, wherein the *Camellia* extract is present in the oral composition about 0.1% to about 0.2% by weight.

20. A method according to claim 18, wherein the oral composition further comprises an antibacterial agent.

21. A method according to claim 18, wherein the anti-bacterial agent is 2',4,4'-trichloro-2-hydroxy-diphenyl ether.

22. A method according to claim 18, further comprising at least one botanical extract selected from the group consisting of magnolia extracts, rosemary extracts, and mixtures thereof.

23. A method according to claim 22, wherein the botanical extract is rosemary extract.

24. An oral care composition comprising:

Camellia extract; and

at least about 0.001% by weight of Vitamin E.

25. A method of at least one of treating and inhibiting an oral inflammatory condition and providing antioxidant activity in an oral cavity by administering to an oral cavity of a human or other animal subject in need thereof an effective amount of an oral composition comprising:

a *Camellia* extract including at least about 30% epigallocatechin gallate, at least about 50% total catechins, and at least about 60% total polyphenols; and

a halogenated diphenyl ether anti-bacterial agent.

26. A method according to claim 25, wherein the *Camellia* extract is present in the oral composition about 0.1% to about 0.2% by weight.

27. A method according to claim 25, wherein the anti-bacterial agent is 2',4,4'-trichloro-2-hydroxy-diphenyl ether.

28. A method according to Claim 25, further comprising at least one botanical extract selected from the group consisting of magnolia extracts, rosemary extracts, and mixtures thereof.

29. A method according to Claim 28, wherein the botanical extract is rosemary extract.

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2005/046242

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K8/97 A61Q11/00

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
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 practical, search terms used)

EPO-Internal, PAJ, WPI Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
X	WO 01/17494 A (THE PROCTER & GAMBLE COMPANY; ZHU, LONG; JI, NING) 15 March 2001 (2001-03-15) page 19 - page 20; claims 1,5,6; examples 5,10	1-29
X	PATENT ABSTRACTS OF JAPAN vol. 011, no. 024 (C-399), 23 January 1987 (1987-01-23) & JP 61 197510 A (SUNSTAR INC), 1 September 1986 (1986-09-01) abstract	1,7-13, 18-20
X	EP 1 072 254 A (SUNSTAR INC) 31 January 2001 (2001-01-31) claims 1,2,5,6,9,10,14; examples 1,3	1-13,18, 19,24
	----- -/--	

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

☒ See patent family annex.

* Special categories of cited documents

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

"E" earlier document 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

26 May 2006

Date of mailing of the international search report

13/06/2006

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Voyiazoglou, D

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2005/046242

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE WPI Section Ch, Week 200512 Derwent Publications Ltd., London, GB; Class A11, AN 2005-109012 XP002382722 & RU 2 241 437 C1 (SVOBODA COSMETICS ASSOC STOCK CO) 10 December 2004 (2004-12-10) abstract -----	1-13,18, 19,24
A	EP 1 002 524 A (MARIE PRATT SARL) 24 May 2000 (2000-05-24) claim 1 -----	1-17,24
A	WO 98/41096 A (D'JANG, ARTHUR, H., K) 24 September 1998 (1998-09-24) claim 1 -----	1-29
A	US 5 683 678 A (HECKERT ET AL) 4 November 1997 (1997-11-04) claims 1,3 -----	1-29
A	WO 2004/073671 A (QUEST INTERNATIONAL SERVICES B.V; BEHAN, JOHN, MARTIN; BRADSHAW, DAVID) 2 September 2004 (2004-09-02) page 16, last paragraph; claim 1 -----	1-29

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2005/046242

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 18-23,25-29 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2005/046242

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0117494	A	15-03-2001	AU 6030299 A CN 1367663 A CN 1373652 A	10-04-2001 04-09-2002 09-10-2002
JP 61197510	A	01-09-1986	JP 1909778 C JP 6035376 B	09-03-1995 11-05-1994
EP 1072254	A	31-01-2001	CA 2330128 A1 WO 9955298 A1 JP 3763075 B2 JP 11302142 A US 6814958 B1	04-11-1999 04-11-1999 05-04-2006 02-11-1999 09-11-2004
RU 2241437	C1	10-12-2004	NONE	
EP 1002524	A	24-05-2000	FR 2763843 A1	04-12-1998
WO 9841096	A	24-09-1998	AT 275826 T AU 6573298 A CA 2283948 A1 DE 69826261 D1 EP 0979037 A1 PT 979037 T	15-10-2004 12-10-1998 24-09-1998 21-10-2004 16-02-2000 28-02-2005
US 5683678	A	04-11-1997	AU 4928396 A CA 2214090 A1 CZ 9702834 A3 EP 0813404 A1 HU 9801240 A2 JP 11501918 T PL 322136 A1 SK 121197 A3 WO 9628135 A1	02-10-1996 19-09-1996 14-01-1998 29-12-1997 28-01-1999 16-02-1999 05-01-1998 06-05-1998 19-09-1996
WO 2004073671	A	02-09-2004	EP 1605909 A1	21-12-2005