

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 07-063441- -00003-0000

Fecha: 2008-08-06 17:14:46 Dep: 2020 NUECREACION
Tra: 11 PATENTEIYII Lve: 378 FASENACIONAL
Act: 538 PETICION Folios: 2

AS. 104.413

Señores

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

DIVISION DE NUEVAS CREACIONES

E. S. D.

REF.: Expediente No. 07 063.441 - Solicitud de Patente FASE NACIONAL

Corresp. a la Solicitud Internacional PCT/US2005/046521.

a nombre de: **COLGATE-PALMOLIVE COMPANY.**

Titulada: COMPOSICIÓN PARA CUIDADO BUCAL ANTIBACTERIANA Y
ANTIINFLAMATORIA.

JUAN PABLO CADENA SARMIENTO, vecino de Bogotá, portador de la tarjeta profesional No. 57492 del Consejo Superior de la Judicatura, obrando como apoderado de la Sociedad **COLGATE-PALMOLIVE COMPANY**, según lo acredita el documento de poder presentado en esa División, de acuerdo con el Artículo 44 de la Decisión 486 de la Comisión de la Comunidad Andina, me permito solicitar que se examine si la invención contenida en la solicitud en referencia es patentable.

De acuerdo con lo anterior, me permito anexar el recibo oficial de caja No. 08-53,444 por valor de \$420.000.

De la Señora Jefe atentamente,

JUAN PABLO CADENA SARMIENTO

C.C. No. 80.410.337 de Usaquén

T.P. No. 57492 del C.S.J.

Cra 7 No. 71-21 Torre B, Piso 4

Bogotá, 06 de agosto de 2008

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DATE	DESCRIPTION	TOTAL COUNTER
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12-3-77	100,000.00	300,000.00
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12-7-77	100,000.00	700,000.00
12-8-77	100,000.00	800,000.00
12-9-77	100,000.00	900,000.00
12-10-77	100,000.00	1,000,000.00
12-11-77	100,000.00	1,100,000.00
12-12-77	100,000.00	1,200,000.00
12-13-77	100,000.00	1,300,000.00
12-14-77	100,000.00	1,400,000.00
12-15-77	100,000.00	1,500,000.00
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12-21-77	100,000.00	2,100,000.00
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12-23-77	100,000.00	2,300,000.00
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12-28-77	100,000.00	2,800,000.00
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1-3-78	100,000.00	3,400,000.00
1-4-78	100,000.00	3,500,000.00
1-5-78	100,000.00	3,600,000.00
1-6-78	100,000.00	3,700,000.00
1-7-78	100,000.00	3,800,000.00
1-8-78	100,000.00	3,900,000.00
1-9-78	100,000.00	4,000,000.00
1-10-78	100,000.00	4,100,000.00
1-11-78	100,000.00	4,200,000.00
1-12-78	100,000.00	4,300,000.00
1-13-78	100,000.00	4,400,000.00
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1-21-78	100,000.00	5,200,000.00
1-22-78	100,000.00	5,300,000.00
1-23-78	100,000.00	5,400,000.00
1-24-78	100,000.00	5,500,000.00
1-25-78	100,000.00	5,600,000.00
1-26-78	100,000.00	5,700,000.00
1-27-78	100,000.00	5,800,000.00
1-28-78	100,000.00	5,900,000.00
1-29-78	100,000.00	6,000,000.00
1-30-78	100,000.00	6,100,000.00
1-31-78	100,000.00	6,200,000.00
2-1-78	100,000.00	6,300,000.00
2-2-78	100,000.00	6,400,000.00
2-3-78	100,000.00	6,500,000.00
2-4-78	100,000.00	6,600,000.00
2-5-78	100,000.00	6,700,000.00
2-6-78	100,000.00	6,800,000.00
2-7-78	100,000.00	6,900,000.00
2-8-78	100,000.00	7,000,000.00
2-9-78	100,000.00	7,100,000.00
2-10-78	100,000.00	7,200,000.00
2-11-78	100,000.00	7,300,000.00
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the 1990s, the number of people in the world who are under 15 years of age is expected to increase from 1.1 billion to 1.5 billion. The number of people aged 65 and over is expected to increase from 200 million to 400 million. The number of people aged 15 and over is expected to increase from 3.5 billion to 4.5 billion. The number of people aged 15 and over is expected to increase from 3.5 billion to 4.5 billion. The number of people aged 15 and over is expected to increase from 3.5 billion to 4.5 billion.

DIVISIÓN DE NUEVAS CREACIONES

RADICACIÓN EXPEDIENTE No. 07-63441

EL EXTRACTO DE LA PRESENTE SOLICITUD DE **PATENTE DE INVENCION**

FUE PUBLICADO EN LA GACETA DE PROPIEDAD INDUSTRIAL No **589** DE

FECHA **29 DE FEBRERO DE 2008** EL TÉRMINO HÁBIL SEÑALADO POR LA

LEY EXPIRA EL **03 DE JUNIO DE 2008**

NOTA: Dentro del plazo de los seis (6) meses siguientes a partir de la fecha de publicación en la gaceta de Propiedad Industrial, deberá solicitar y cancelar el examen de patentabilidad so pena de que la solicitud caiga en abandono, de acuerdo con lo establecido en el Artículo 44 de la Decisión 486/2000.

SE PRESENTARON OPOSICIONES POR PARTE DE TERCEROS.

SI _____

NO X



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : A61K 35/78, 7/26	A1	(11) International Publication Number: WO 97/35599 (43) International Publication Date: 2 October 1997 (02.10.97)
(21) International Application Number: PCT/KR97/00048 (22) International Filing Date: 26 March 1997 (26.03.97) (30) Priority Data: 1996/8393 26 March 1996 (26.03.96) KR (71) Applicant (for all designated States except US): DAEWOONG PHARMACEUTICAL CO., LTD. [KR/KR]; 223-23, Sangdaewon-dong, Joongwon-ku, Sungnam-city, Kyunggi-do 462-120 (KR). (72) Inventors; and (75) Inventors/Applicants (for US only): CHUNG, Chong-Pyoung [KR/KR]; Kaepo Woosung 4th Apartment, 3-307, Dogok 2-dong, Kangnam-ku, Seoul 135-272 (KR). BAE, Ki-Hwan [KR/KR]; 113-12, Goojeong-dong, Seo-ku, Daejeon 302-200 (KR). CHUNG, Chong-Keun [KR/KR]; Mu-goonghwa Apartment, 122-1801, Keumjeong-dong, Kunpo-city, Kyunggi-do 435-050 (KR). (74) Agents: CHOI, Kyu, Pal et al.; 824-20, Yeoksam-dong, Kangnam-ku, Seoul 135-080 (KR).		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published With international search report.

(54) Title: COMPOSITION FOR PREVENTION AND TREATMENT OF PERIODONTAL DISEASES



(57) Abstract

The present invention relates to a composition for the prevention and treatment of periodontal disease. More specifically, the present invention relates to a composition for the prevention and treatment of periodontal disease comprising an extract of Zizyphi fructus and an extract of Magnoliae cortex. When the extract of Zizyphi fructus and the extract of Magnoliae cortex are combined in the weight ratio ranging from 1:6 to 1:12 and, preferably from 1:8 to 1:10, they together show a synergistic effect in comparison to the single use of any one of them, alone, and further exhibit an excellent effect for treatment of periodontal diseases in comparison with the agents disclosed in the prior art for prevention and treatment of periodontal diseases.

Ginkgo folium is effective against periodontal diseases and, indeed, have filed a patent application relating to a composition for treatment of periodontal diseases comprising just such a combination (see, Korean Patent Application No. 94-14117). As a result of still further study, the present inventors have also identified that the extract of Zizyphi fructus is effective for regenerating periodontal tissues, and have filed a patent application relating to an agent for treatment of periodontal disease comprising the extract of Zizyphi fructus (see, Korean Patent application No. 95-14541).

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Although the extract of Magnoliae cortex displays good anti-inflammatory and antibacterial activities, it has the disadvantage of lowering the activity of periodontal tissue cells as its dosage increases. Meanwhile, the extracts of Zizyphi fructus and Ginkgo folium together exhibit a good tissue regenerating effect but also have a weak antibacterial effect. Therefore, they are disadvantageous in view of the fact that they exhibit the effect through only some ways among various mechanisms involved in the prevention and treatment of periodontal diseases.

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On the basis of the result of previous studies mentioned above, the present inventors have examined the efficacy of various combinations of the extracts of Magnoliae cortex and Zizyphi fructus for preventing and treating periodontal diseases. As a result, we have discovered that the combination of these two extracts at certain weight ratios shows a unexpected synergistic effect for treating periodontal diseases (i.e. excellent tissue regenerating, antibacterial and anti-inflammatory effects) and overcomes the disadvantage of the extract of Magnoliae cortex alone (i.e. inhibits the activity of periodontal tissue cells at high dosage) to provide a good tissue regenerating effect. Then, we have completed the present invention.

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DISCLOSURE OF INVENTION

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The present invention relates to a composition comprising the

extract of *Zizyphi fructus* and the extract of *Magnoliae cortex* as its effective components which, at certain weight ratios of its active components, is broadly effective for preventing and treating periodontal diseases (i.e. exhibits (1) a regenerative effect on weakened or disrupted periodontal tissues, (2) an inhibitory effect on the inflammatory response which disrupts the periodontal tissues, and (3) an antibacterial effect on causative organisms of periodontal diseases) and which is far more effective than each of the extracts of *Zizyphi fructus* and *Magnoliae cortex* alone. In addition, the composition of the present invention has the additional advantage that it has no harmful side effects such as those exhibited by antibiotics of the prior art.

BRIEF DESCRIPTION OF DRAWINGS

For a thorough understanding of the nature and objects of the invention, reference should be made to the following detailed description taken in connection with the accompanying drawings in which:

Figure 1 is a photograph ($\times 40$) of the calvaria of a mouse of the fifth group, which was used as the negative control group according to Experiment 4, 2 weeks after the defect operation. This photograph shows that at both sides of the defected portion having diameter of 5mm in the calvaria some new bone has formed in line but that the whole defected portion has filled with fibrous connective tissues.

Figure 2 is a photograph ($\times 40$) of the calvaria of a mouse of the third group (unsaponified extract of *Zea mays*, 0.1g/kg), which was used as the positive control group according to Experiment 4, 2 weeks after the defect operation. This photograph shows that most of the defected portion having diameter of 5mm in the calvaria has filled with fibrous connective tissues and that new bone and bone-like tissues have formed around the existing defected bone tissue.

Figure 3 is a photograph ($\times 40$) of the calvaria of a mouse of the fourth group (unsaponified extract of *Zea mays*, 0.5g/kg), which was used

BEST MODE FOR CARRYING OUT THE INVENTION

In the composition of the present invention, the extract of Magnoliae cortex is best obtained by extracting Magnoliae cortex with an alcohol, preferably with a lower alkanol such as ethanol. It is also preferable to use an extract of Magnoliae cortex containing at least 5.0% of magnolol and at least 1.0% of honokiol as its major ingredients. In addition, the extract of Zizyphi fructus is best obtained by extracting Zizyphi fructus with an alcohol, preferably with a lower alkanol such as ethanol, in a water bath and then concentrating the extract under reduced pressure.

The composition comprising the extracts of Zizyphi fructus and Magnoliae cortex as its active components according to the present invention exhibits a surprising synergistic effect for treating periodontal diseases when these extracts are present in specific proportions. Specifically, as demonstrated by the experiments detailed below, a synergistic effect is evident when the ratio of the weight of the extract of Zizyphi fructus to the weight of the extract of Magnoliae cortex ranges from 1:6 to 1:12, and preferably from 1:8 to 1:10.

Therefore, to maximize the synergistic therapeutic effect on periodontal diseases the composition of the present invention uses the extract of Zizyphi fructus and the extract of Magnoliae cortex in the mixing ratio ranging from 1:6 to 1:12, particularly preferably in the mixing ratio ranging from 1:8 to 1:10, on the basis of weight.

Although the composition of the present invention comprising the extracts of Zizyphi fructus and Magnoliae cortex in the mixing ratios mentioned above may be used as composed, the composition would preferably be used in pharmaceutical preparations formulated by adding conventional pharmaceutically acceptable excipients to the composition. The pharmaceutical preparations used for this purpose include tablets, ointments, solutions (gargles), sprays, etc. For example, the composition of the present invention may be included in the toothpaste or formulated

as tablets for internal use, ointments for external use, or solutions by mixing the extracts with pharmaceutically acceptable carriers.

In addition, the composition of the present invention may be included in conventional gargle preparations for washing the mouth, or it may be mixed with a propellant to prepare a spray packaged in a pressurized container and then sprayed onto the attacked periodontal portion, or it may be included in toothpaste which is used over a long period of time to obtain the preventive and therapeutic effect on periodontal diseases.

The effective dosage of the present composition can be varied depending on the purpose of use, the severity of periodontal disease to be treated, the preparation employed, etc., but is generally from 50mg to 5g, particularly from 100mg to 3g, per day for an adult man, as the combination of the extracts of *Zizyphi fructus* and *Magnoliae cortex*.

The content of the combination of the extracts of *Zizyphi fructus* and *Magnoliae cortex* in the total composition may be varied depending on the purpose of its use. However, when the content of the active ingredients is too low, the pharmaceutical effect of the composition rapidly decreases, whereas when their content is too high, the quality of the product may be reduced due to the colouring effects of the extracts of *Zizyphi fructus* and *Magnoliae cortex*. Based on the effective dosages given above, it is preferable to formulate the unit dosage form so that a tablet contains from 50mg to 250mg of the combination of the present invention and the ointment, solution (gargle), toothpaste and spray contain the combination of the present invention in the concentration of 0.2 to 5.0 wt%.

When the extracts of *Zizyphi fructus* and *Magnoliae cortex* are orally administered to mice and rats, the LD₅₀ level of each extract, which was used as the standard of acute toxicity, was determined to be 5000mg/kg or more. It is therefore evident that they are safe medicinal substances.

WHAT IS CLAIMED IS :

1. A composition for the prevention and treatment of periodontal diseases which comprises an alcohol extract of Zizyphi fructus and an alcohol extract of Magnoliae cortex wherein the ratio of the weight of the extract of Zizyphi fructus to the weight of the extract of Magnoliae cortex ranges from 1:6 to 1:12.
2. The composition as defined in claim 1, wherein the ratio of the weight of the alcohol extract of Zizyphi fructus and the weight of the alcohol extract of Magnoliae cortex ranges from 1:8 to 1:10.
3. The composition as defined in claim 1 or 2, wherein the alcohol extract of Zizyphi fructus and the alcohol extract of Magnoliae cortex are ethanol extracts thereof.
4. The composition as defined in claim 1, which is formulated in a pharmaceutical unit dosage form using an additional pharmaceutically acceptable carrier.
5. The composition as defined in claim 4, wherein the pharmaceutical unit dosage form is tablet, ointment, toothpaste, solution (gargle) or spray.
6. The composition as defined in claim 5, which contains from 50mg to 250mg of the combination of the extract of Zizyphi fructus and the extract of Magnoliae cortex per tablet.
7. The composition as defined in claim 5, which contains the combination of the extract of Zizyphi fructus and the extract of Magnoliae cortex in the concentration of 0.2 to 5.0 wt% per unit dosage form of ointment, toothpaste, solution (gargle) or spray.



US005370863A

United States Patent [19]
Barney et al.

[11] **Patent Number:** **5,370,863**
 [45] **Date of Patent:** **Dec. 6, 1994**

- [54] **ORAL CARE COMPOSITIONS
 CONTAINING HOP ACIDS AND METHOD**
- [75] **Inventors:** Michael C. Barney, Elm Grove;
 Edward J. Kot, Delafield; Etzer
 Chicoye, Milwaukee; Janna K. Jilek,
 West Allis, all of Wis.
- [73] **Assignee:** Miller Brewing Company,
 Milwaukee, Wis.
- [21] **Appl. No.:** 991,613
- [22] **Filed:** Dec. 16, 1992
- [51] **Int. Cl.⁵** A61K 7/26
- [52] **U.S. Cl.** 424/49; 424/76.1;
 424/76.8; 424/76.9; 426/600
- [58] **Field of Search** 424/49, 76.1, 76.8,
 424/76.9; 426/600

[56] **References Cited**
U.S. PATENT DOCUMENTS

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5,200,227	4/1993	Guzinski et al.	426/600

FOREIGN PATENT DOCUMENTS

1112182 11/1981 Canada .

Primary Examiner—Thurman K. Page
Assistant Examiner—Robert H. Harrison
Attorney, Agent, or Firm—Quarles & Brady

[57] **ABSTRACT**

Oral care compositions containing hop acids or their salts are effective in inhibiting Gram positive bacteria which can cause plaque or periodontal disease. A representative composition is a toothpaste containing tetrahydroisohumulone.

2 Claims, No Drawings

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ORAL CARE COMPOSITIONS CONTAINING HOP
ACIDS AND METHOD

FIELD OF THE INVENTION

This invention relates to oral care compositions which contain hop acids and to a method for inhibiting undesirable Gram positive microorganisms in the oral cavity.

BACKGROUND OF THE INVENTION

It is generally believed that bacterial plaque is directly associated with dental caries and periodontal disease. Plaque is formed by a combination of events starting with a salivary coating which forms on the teeth to which various forms of *Streptococcus* adhere. The Gram positive *Streptococcus*, principally *S. mutans* and *S. sanguis*, with the assistance of bacterially produced enzymes form dextrans from sucrose which is in the oral cavity. The dextrans serve as nutrients which support the growth of additional organisms which produce acids which can demineralize both enamel and dentin and cause dental caries and decay. In addition to dental caries, gingivitis and other periodontal diseases are known to be caused by bacteria.

It was known in the brewing industry that some hop acids can inhibit the growth of the microorganisms that can cause spoilage in beer. For example, the Todd Jr. et al. U.S. Pat. No. 5,082,975 discloses that the hop acid, hexahydrocolupulone, can inhibit the growth of certain *Lactobacillus*. However, no literature or patents of which we are aware disclose or suggest that hop acids might be useful to inhibit the microorganisms that cause dental caries and periodontal disease.

BRIEF SUMMARY OF THE INVENTION

It is an object of the present invention to disclose novel oral care compositions which inhibit the microorganisms that cause plaque and periodontal disease.

It is also an object to disclose a method of inhibiting plaque and periodontal disease employing the novel compositions of the present invention.

The novel oral care compositions of the present invention are those which contain the hop acids, tetrahydroisohumulone, tetrahydroisoadhumulone, tetrahydroisocohumulone, Rho-isohumulone, Rho-isoadhumulone, Rho-isocohumulone, lupulone, adlupulone, colupulone, hexahydrolupulone, hexahydroadlupulone, hexahydrocolupulone, mixtures thereof, and the salts thereof, in combination with suitable pharmaceutically acceptable carriers.

The novel oral care compositions of the present invention are toothpastes, tooth powders, mouthwashes, gums and the like which are formulated for administration to the oral cavity. Normally, such compositions will contain about 1.0 to 100 parts per million (ppm) or about 0.0001-0.0100% weight percent of one or more hop acids or their salts.

The novel method of inhibiting undesirable gram positive microorganisms in the oral cavity basically comprises introducing a novel oral care composition of the present invention into the oral cavity so that the hop acid(s) can inhibit the Gram positive microorganisms that may be present. The spent composition is then preferably removed, however, it can be ingested without any detrimental effects because of the proven safety of the hop acids.

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It will be apparent to those skilled in the art that the above described and additional objects and advantages may be obtained by the practice of the present invention.

DETAILED OF THE PREFERRED
EMBODIMENTS

The preferred oral care compositions are those which contain a safe and effective amount of a hop acid or a mixture thereof and/or the salts thereof in combination with a pharmaceutically acceptable carrier suitable for use in the oral cavity.

The preferred compositions of the present invention are formulated for use in the oral cavity without being ingested, except for ingestion that might incidentally occur during usage. In the preferred method of use, the composition will be administered to the oral cavity, kept there during treatment and subsequently removed when treatment is finished.

The phrases "oral administration" and "administered to the oral cavity," as used herein are meant to describe any method by which the compositions of the present invention are administered into the mouth and contacted with the teeth and gums. Such methods basically comprise bringing the compositions into contact with the teeth and gums, as well as with any calculus or plaque that may be present or form in the oral cavity. The contact may occur by rinsing, brushing with a toothbrush, bringing a solution containing the composition into contact with the teeth and/or gums.

The "oral compositions" of the present invention include powders, pastes, gels, solutions, and the like, for rinsing, brushing, washing or topical application in the oral cavity. These compositions include compositions for cleaning teeth, prophylactic compositions, such as antigingivitis compositions, and mouth rinses and other oral care compositions. The compositions may contain as active ingredients only the hop acids or may contain the hop acids in combination with other dentifrice, prophylactic, and oral care ingredients.

The phrase "pharmaceutically acceptable carrier" is intended to mean one or more hop acid-compatible solid or liquid diluents or encapsulating substances which are suitable for oral administration, such as application to or rinsing of the oral cavity e.g., mouth.

The concentration of the hop acid(s) in the oral care compositions should be at least an effective amount for providing the desired utility (i.e., calculus-inhibiting utility or plaque-inhibiting utility). While the total concentration of the hop acids in the oral composition can be between about 1.0 to 100 ppm or 0.0001 to 0.100 %, by weight, generally an oral care composition will contain between about 10 and 50 ppm, of the hop acid(s) or salts.

By "safe and effective amount" as used herein is meant an amount of a hop acid or salt thereof which is enough to provide anticalculus and/or antiplaque efficacy, preferably both, but not so high as to fall outside the scope of sound medical judgement. The safe and effective amount can vary with the particular hop acid chosen, the intended use of the composition, the duration of treatment, and the particular carrier with which the hop acid is combined. Generally the amount of the hop acid administered on a regular basis, in the form of the described oral compositions is an amount which is effective to inhibit the microorganisms without being too bitter.

The oral care compositions of the present invention preferably have a pH of between about 5.0 and about 9.0. A preferred pH range is about 7.0 to about 9.0. The compositions will be buffered, for example, by including a buffer in the carrier so that a pH of between about 5.0 and about 9.0 is maintained in the oral cavity during use. Exemplary nonlimiting buffers include citrate, citrate/bicarbonate, and phosphate buffers.

The carrier also can contain the usual components of the particular type of oral compositions desired. Such additional components can include abrasives, sudsing agents, flavoring agents, sweetening agents, coloring agents, pigments, humectants, binders (thickening agents), other anticaries agents, etc. The choice of carrier to be used is basically determined by the way the composition is to be introduced to the oral cavity and by the purposes for which the composition is meant to be effective. For example, if a toothpaste is to be used, then a "toothpaste carrier" is chosen containing abrasive materials, sudsing agents, binders, humectants, flavoring and sweetening agents, etc. If a mouth rinse is to be used, then a "mouth rinse carrier" containing water, flavoring and sweetening agents, possibly an organic solvent such as ethanol, etc. is chosen. Similarly, if a chewing gum is to be used, then a conventional "chewing gum carrier" containing gum base, flavoring and sweetening agents is chosen. Other carriers suitable for the preparation of the oral care compositions of the present invention are well known in the art.

Other active ingredients also can optionally be added to the compositions of this invention. Suitable antiplaque agents may include bis-biguanide compounds such as chlorhexidine (1,6-bis [N⁵-p-chlorophenyl-N'-biguanido]hexane), the soluble and insoluble salts thereof, and related materials such as 1,2-bis(N⁵-p-trifluoromethylphenyl-N'-biguanido)ethane. The composition of the present invention also can contain other anticalculus agents, or antitartar agents, such as the dialkali metal and mixtures of dialkali metal and tetraalkali metal pyrophosphate salts. If present, the op-

tional antiplaque agents generally comprise from about 0% to about 5% by weight of the compositions herein.

The topical solutions and mouth rinses herein also may contain ethanol in an amount preferably of from about 0% to about 30%.

Water can also be present in the compositions of this invention. Water employed in the preparation of commercially suitable dentifrices, prophylactic compositions, and other oral care compositions should preferably be deionized and free of organic impurities. Water generally comprises from about 10% to 50%, preferably from about 20% to 40%, by weight of the toothpaste compositions herein. Mouth rinses generally contain from about 45% to about 95% water. These amounts of water include the free water which is added plus that which is introduced with other materials such as with sorbitol.

It is common to have a water-soluble fluoride compound present in dentifrices in an amount sufficient to give a fluoride concentration of from about 0.0025% to about 5.0% by weight, preferably from about 0.005% to about 2.0% by weight, to provide additional anticaries efficacy. Preferred fluorides are sodium fluoride, stannous fluoride, indium fluoride, and sodium monofluorophosphate.

The preferred hop acids ingredient of the oral compositions of the present invention is a mixture of tetrahydroisohumulone, tetrahydroisoadhumulone and tetrahydroisocohumulone. Other hop acid ingredients that can be used include Rho-isohumulone, Rho-isoadhumulone, Rho-isocohumulone, isohumulone, isoadhumulone, isocohumulone, lupulone, adlupulone, colupulone, hexahydrolupulone, hexahydroadlupulone, hexahydrocolupulone, the salts thereof and mixtures thereof.

The results of tests demonstrating the antimicrobial action of various mixtures of hop acids on microorganisms, including *S. mutans* and *S. sanguis*, are shown in Table 1.

TABLE 1

SUMMARY OF THE MINIMAL INHIBITORY CONCENTRATIONS (PPM) OF HOP COMPOUNDS ON VARIOUS MICROORGANISMS

Test Organism	Hop Acid Mixture			
	Tetrahydro-isohumulones	Rho-isohumulones	Hexahydro-colupulones	Colupulones
Gram Positive Bacteria				
<i>Pediococcus</i> RB1	>8<16 ^a	>125<250	none ^b	none
<i>Pediococcus</i> RB2	>16<32	>63<125	none	— ^c
<i>Pediococcus</i> EP-404A	>4<8	>32<63	none	—
<i>Lactobacillus delbrueckii</i> PEL	>63<125	>63<125	none	none
<i>Lactobacillus plantarum</i> KGF50	>32<63	>125<250	none	none
<i>Lactobacillus plantarum</i> KGF54	>32<63	>63<125	none	none
<i>Micrococcus</i> PRT	>16<32	>16<32	>3.2<6.3	>12.5<25
<i>Staphylococcus aureus</i>	>16<32	>16<32	none ^b	>6.3<12.5
<i>Streptococcus pyogenes</i>	>1<2	>16<32	none	none
<i>Streptococcus pneumoniae</i>	>4<8	>8<16	>0.2<0.4	>25<50
<i>Streptococcus faecalis</i>	>32<63	>63<125	none	none
<i>Streptococcus mutans</i>	>4<8	— ^c	>12.5<25	>8<16
<i>S. sanguis</i>	>13<25	— ^c	—	>25<50
<i>Bacillus cereus</i>	>16<32	>4<8	>1.6<3.2	>0.8<1.6
<i>Bacillus subtilis</i>	>8<16	>8<16	>0.8<1.6	>3.2<6.3
<i>Listeria monocytogenes</i> ScottA	>8<16	>8<16	>0.4<0.8	>12.5<25
<i>Listeria innocua</i>	—	—	>0.8<1.6	—

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TABLE 1-continued

Test Organism	Hop Acid Mixture			
	Tetrahydro- isohumulones	Rho- isohumulones	Hexahydro- colupulones	Colupulones
<i>Listeria seeligeri</i>	—	—	>0.4<0.8	—
<i>Propionibacterium acnes</i>	>8<16	>8<16	>4<8	>32<64
^a greater than 8 but less than 16 inhibited ^b "none" = none of the concentrations tested were found to be inhibitory ^c — = not tested				
Gram Negative Bacteria				
<i>Escherichia coli</i>	none ^a	none	none	none
<i>Salmonella typhimurium</i>	none	none	— ^b	—
<i>Pseudomonas aeruginosa</i>	none	none	—	—
<i>Candida albicans</i>	none	none	none	none
^a "none" = none of the concentrations tested were found to be inhibitory ^b — = not tested				

-continued

Ingredient	% w/w
Distilled Water q.s. ad.	100.00

The practice of the present invention is further illustrated by the examples which follow:

EXAMPLE 1

The following is a representative example of a toothpaste that could be made employing the teachings of the present invention.

Ingredient	% w/w
Sorbitol (70% Aqueous Solution)	49.56
Sodium Saccharin	0.30
Dye Solution	0.35
Precipitated Silica	20.00
Sodium Fluoride	0.25
Flavor	1.30
Sodium Alkyl Sulfate (27.9% Aqueous Solution)	5.00
Carbopol 940	0.20
Xanthan Gum	0.60
Tetrahydroisohumulone (25 ppm)	0.0025
Distilled Water q.s. ad.	100.00

The above composition would be made by combining the water and part of the sorbitol in an agitated mixture and heating this mixture to 140° F. The tetrahydroisohumulone [in ethanol solution], saccharin, sodium fluoride and precipitated silica would then be added in order and the total mixture mixed for from 5 to 10 minutes. The flavor, dye and surfactant would then be added. In a separate vessel the remainder of the sorbitol, the Carbopol and the xanthan gum would be slurried together and then added to the main mix tank. The complete batch would then be mixed for about one-half hour and subsequently milled and deaerated.

EXAMPLE 2

The following is another representative toothpaste which could be made employing the teachings of the present invention.

Ingredient	% w/w
Sorbitol (70% Aqueous Solution)	50.75
Sodium Saccharin	0.30
Dye Solutions	0.35
Precipitated Silica	20.00
Sodium Fluoride	0.25
Flavor	1.30
Sodium Alkyl Sulfate (27.9% Aqueous Solution)	5.00
Carbopol 940	0.20
Xanthan Gum	0.60
Rho-isohumulone	0.0050

The toothpaste could be prepared as described in Example 1.

- 25 In addition to the levels and combinations of ingredients shown in these examples, others might be used which are consistent with the invention disclosed.

EXAMPLE 3

- 30 The following is an example of a mouth rinse composition which could be made employing the teachings of the present invention.

Ingredient	%
Tetrahydroisohumulone	0.0025
Ethanol	16.25
Glycerin	10.00
Nonionic Surfactant	0.12
Benzoic Acid	0.05
Sodium Saccharin	0.05
Flavor	0.15
Color	0.04
Sodium Hydroxide (10% sol.)	0.15
Distilled Water q.s. ad.	100.00

- 45 The mouth rinse would be prepared by adding each of the ingredients to the distilled water with stirring until a solution is obtained.

The salts of the hop acids which can be used to prepare the oral care compositions of the present invention are preferably the sodium and potassium salts. They are easily prepared and quite soluble. The salts may be preferred when it is desired to make an oral care composition without adding alkali buffering agents.

- 50 It will be readily apparent to those skilled in the art that an number of modifications and changes can be made without departing from the spirit and scope of the invention. Therefore, it is intended that the invention be limited only by the claims.

We claim:

- 60 1. An oral care composition selected from a toothpaste and tooth power, said composition comprising about 0.0001 to 0.0100% by total weight of a compound which inhibits *Streptococcus mutans*, said compound being selected from the group consisting of tetrahydroisohumulone, tetrahydroisadhumulone, tetrahydroisocohumulone and mixtures thereof.

- 65 2. An oral care composition of claim 1 in which the composition is a toothpaste containing tetrahydroisohumulone.

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