



No. 07-058653- -00003-0000

Fecha: 2008-08-19 16:42:48 Dep 2020 NUECREACIONE
Ira. 11 PATENTE IYII Eve: 378 FASE NACIONAL
Act. 538 PETICION Folios: 2

AS. 104.223

Señores

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

DIVISION DE NUEVAS CREACIONES

E. S. D.

REF.: Expediente No. 07 058.653 - Solicitud de Patente FASE NACIONAL

Corresp. a la Solicitud Internacional PCT/US2005/040568.

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

Titulada: COMPOSICIÓN PARA EL CUIDADO BUCAL Y CONTROL DEL SARRO
QUE CONTIENE EXTRACTO DE MAGNOLIA.

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. 08-53,440 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, 19 de agosto de 2008

MEV/CAG/jpg

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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

NIT : 900176089-2

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 07-058653- -00003-0000

RECIBO OFICIAL DE CAJA : 08 - 53,440
FECHA : JULIO 7 DE 2008Fecha: 2008-08-19 16:42:48 Dep. 2020 NUECREACION
Tra. 11 PATENTEIYII Eve: 378 FASENACIONALI
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***** CONSIGNACION *****

DEPOSITANTE	TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PAGO	Vr. PAGO
BRIGARD & CASTRO LTDA	CONSIGNACION	BANCO DE BOGOTA	062754387	3249794	07/07/2008	17,750,000.00

***** CONCEPTO *****

CANT.	RENTISTICO	CONCEPTO	TOTAL CONCEPTO
1	50005-01-01	SOLICITUDES	
		85 EXAMEN DE PATENTABILIDAD DE INVEN	420,000.00
		TOTAL :	\$ 420,000.00

SDN: CUATROCIENTOS VEINTE MIL PESOS

RESPONSABLE : _____

RECIBO DE CAJA APLICADO AL EXPEDIENTE No. _____

DIVISIÓN DE NUEVAS CREACIONES

RADICACIÓN EXPEDIENTE No. 07-58653

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

FUE PUBLICADO EN LA GACETA DE PROPIEDAD INDUSTRIAL No **590** DE

FECHA **31 DE MARZO DE 2008** EL TÉRMINO HÁBIL SEÑALADO POR LA LEY

EXPIRA EL **27 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



US006500409B1



(12) **United States Patent**
Scherl et al.

(10) **Patent No.:** **US 6,500,409 B1**
(45) **Date of Patent:** **Dec. 31, 2002**

(54) **SYNERGISTIC ANTIPLAQUE/
ANTINGIVITIS ORAL COMPOSITION**

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(*) Notice: Subject to any disclaimer, the term of this
patent is extended or adjusted under 35
U.S.C. 154(b) by 0 days.

(21) Appl. No.: **09/568,114**

(22) Filed: **May 10, 2000**

(51) Int. Cl.⁷ **A61K 7/26**; A61K 7/16;
A61K 35/78

(52) U.S. Cl. **424/58**; 424/49; 424/195.1

(58) Field of Search 424/49-58, 195.1

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,537,996 A * 8/1985 Kooda et al. 568/442
5,032,386 A * 7/1991 Gaffar et al. 424/49
5,080,887 A * 1/1992 Gaffar et al. 424/52
5,135,746 A * 8/1992 Matsuno et al. 424/195.1
5,188,821 A 2/1993 Gaffar et al. 424/52
5,288,480 A * 2/1994 Gaffar et al. 424/52

FOREIGN PATENT DOCUMENTS

CN 1094895 A * 11/1994
CN 1096699 A * 12/1994
JP 57085319 A2 * 5/1982
JP 01151512 A * 6/1989
JP 10152426 A * 6/1998
JP 2001010904 A * 1/2001

WO 9735599 10/1997 A61K/35/78

OTHER PUBLICATIONS

Ho Et Al Phyto Ther. Res. 15(2): 139-141 Honokiol/Mag-
nolol MIC 25.Mu G/ml., 2001.*

Mao Et Al Zhongguo Gonggong Weisheng Xuebao 18(4):
215-216 H/M: MBC 16.Mu G/ml., 1999.*

Namba Et Al Wakanyaku Shinpojumu 15:179-186 M/H
MIC 6.3 Mu G/ml, 1982.*

Namba Et Al Planta Med 44(2): 100-106 M/A: MIC 6.3 Mu
G/ml., 1982.*

Namba Et Al Shoya Kugaku Zasshi 36(3):222-227 M/H :
MIC 12.5.25Mug/m., 100 Mug/ml, 1982.*

Chang Et Al Planta Med 64(4) : 367-369 M/H, 1998.*

Bae Et Al Yakhak Hoechi 35(1): 7-10 Syn, 1991.*

Seo Et Al. Arch. Pharmacol. Res. 9(3):127-130 Syn, 1986.*

Bae Et Al Saengyak Hakhoechi 17(1)-85-90 Syn, 1986.*

Hattori Et Al Shoya Kusaku Zasshi: 39(1):76-79 Syn,
1985.*

Yoo Et Al Haksul Yongveah 8(2):207-212 M H, 1981.*

Ito Et Al Chem Pharm Bull 30(9):3347-3383 Syn, 1982.*

Dental Caries Prevention by Traditional Chinese Medi-
cines—Part II—Potential Antibacterial Action of Magnoliae
Cortex Extracts against *Streptococcus Mutans*, Journal of
Medicinal Plant Research—1982, vol. 44, pp. 100-106.

* cited by examiner

Primary Examiner—Shep K. Rose

(74) *Attorney, Agent, or Firm*—Paul Shapiro

(57) **ABSTRACT**

An oral care composition containing a synergistic
antiplaque/antigingivitis combination of a nonionic haloge-
nated diphenyl ether compound such as Triclosan and an
extract of Magnolia Officinalas containing honokiol and
magnolol.

10 Claims, No Drawings

SYNERGISTIC ANTIPLAQUE/ ANTINGIVITIS ORAL COMPOSITION

BACKGROUND OF THE INVENTION

1. Field of the Invention

This invention relates to a antiplaque combination of a noncationic halogenated hydroxydiphenyl ether antibacterial agent and an extract of *Magnolia Officinalis* and more particularly to an oral composition containing such combination which exhibits increased antingivitis effect due to synergistic antibacterial effect against plaque bacteria.

2. The Prior Art

It is difficult to predict the antiplaque efficacy of antibacterial compounds when incorporated in a delivery vehicle and particularly in oral compositions. For example, dental plaque is a soft deposit which forms on teeth as opposed to calculus which is a hard calcified deposit on teeth. Unlike calculus, plaque may form on any part of the tooth surface, particularly at the gingival margin and is implicated in the occurrence of gingivitis. Cationic antibacterial compounds such as chlorhexidine, benzothonium chloride and cetyl pyridinium chloride have been used by the art as antibacterial antiplaque agents in oral compositions. However, such agents are generally not effective when there is also present in the oral composition an anionic surfactant required for the effective performance of oral compositions such as toothpaste and mouthrinses.

Noncationic antibacterial materials are compatible with anionic surfactants in oral compositions and noncationic halogenated hydroxydiphenyl ethers such as Triclosan have been effectively employed in commercial oral compositions as antiplaque agents when mixed with neutral ingredients such as humectants, abrasives and thickeners conventionally used in the formulation of oral compositions. Notwithstanding the efficacy of halogenated hydroxydiphenyl ethers such as Triclosan, there is a continuing interest in the oral care field for agents which improve the efficacy of such noncationic halogenated hydroxydiphenyl ethers.

Recently, interest has been displayed in the medicinal properties of herbal preparations for use in oral compositions. Herbal preparations are considered "more natural" and are therefore viewed as more acceptable antibacterial ingredients to the consumer.

Extracts of *Magnolia Cortex* (barks of *Magnolia officinalis*) are known to have antibacterial efficacy. For example, it has been reported in "Dental caries Prevention by Traditional Chinese Medicines", T. Namba et al, J. Medicinal Plant Res., vol. 44, pp. 100-106(1982) that some active principles of these extracts, identified to be magnolol and honokiol, were bactericidal against *S. mutans* in the in vitro test Minimal Inhibitory Concentration (MIC) but was not found to be inhibitory to plaque adherence to teeth in vitro tests designed to determine the therapeutic efficacy of antiplaque antingivitis.

The dental art is continuously seeking synergistic enhancement of antiplaque/antigingivitis of non-herbal, antibacterial compositions such as halogenated biphenylether using herbal compositions in which the non-herbal ingredient has high antibacterial activity alone, while the herbal ingredient has little or no antiplaque activity, wherein the two ingredients have far higher antiplaque activity than could be expected from their individual activities, thus displaying synergism. The advantage of such synergism is that the effectiveness of the non-herbal antiplaque agent is

greatly increased, without a concomitant increase in the dosage level or rate of administration so that lower quantities of the non-herbal antiplaque agent can be administered, yet still achieve the desired therapeutic effect. Such synergistic combinations are particularly important in the treatment of delicate or sensitive tissues, such as the oral mucosa, where the ability to reduce the level of the non-herbal antiplaque agent in the oral composition would be beneficial.

There is thus a recognized need for, and it would be highly advantageous to have a antiplaque dentifrice in which a combination of a non-herbal antiplaque agent and a herbal ingredient exhibited synergistic antiplaque activity resulting into enhanced effectiveness against gingivitis.

SUMMARY OF THE INVENTION

In accordance with the present invention it has been unexpectedly discovered that a combination of a nonionic halogenated hydroxydiphenyl ether such as Triclosan and phenolic compound selected from magnolol and honokiol and mixtures thereof extracted from the cortex of *Magnolia Officinalis* hereinafter referred to as "Magnolia Extract", are synergistically effective in inhibiting the growth of plaque causing bacteria whereby enhanced antiplaque activity in substantial excess of the additive antibacterial effect of the individual noncationic halogenated hydroxydiphenyl ether or *Magnolia Extract* is exhibited by the combination of these agents.

The fact that halogenated hydroxydiphenyl ether compounds such as Triclosan have been approved as safe and effective for use in oral care products and that the *Magnolia Extract* is a widely used herbal extract, particularly in Chinese medicine, suggests that these compounds will both be commercially acceptable as ingredients in oral hygiene products such as dentifrice, mouth rinse, chewing gum and lozenge formulations.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

The *Magnolia Extract* of the present invention is a dried cortex extract of *Magnolia officinalis* which belongs to the family Magnoliaceae. As used herein, "extracting" or "extraction" of a solid or liquid material means contacting the material, which if solid is preferably dried and crushed or ground, with an appropriate solvent to remove the substance(s) desired to be extracted from the material. Such an extraction may be carried out by conventional means; for example, by using an extraction apparatus, such as a Soxhlet apparatus, which retains the solid material in a holder and allows the solvent to flow through the material; or by blending the solvent and material together and then separating the liquid and solid phases or two immiscible liquid phases, such as by filtration or by settling and decanting.

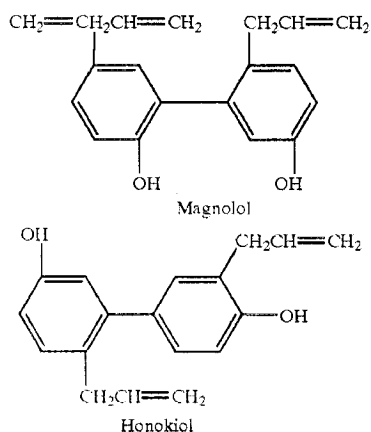
Preferred *Magnolia Extracts* used in the practice of the present invention are made from dried *Magnolia* plant bark and can be prepared by extracting the bark using an appropriate solvent. Preferred solvents include methanol, ethanol, methylene chloride, hexane cyclohexane, pentane, petroleum ether, chloroform and ethylene dichloride, one part of plant tissue (dry basis) is extracted with from about 5 to about 50 parts, preferably from about 15 parts to about 30 parts of solvent using an extraction apparatus where the solvent is contacted with the bark to obtain a concentrated paste which is then subjected to one or more additional extraction steps with different solvents to further concentrate the originally obtained paste over an extended period of

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time, preferably from about 6 hours to about 1–2 days, more preferably for about 1 day.

In one method of extraction, the dried, crushed Magnolia bark in the form of a powder is sequentially contacted with ethanol, methylene chloride, and cyclohexane to form in each step a concentrated paste, the last paste form being dissolved in heated petroleum ether at about 50°–60° C. and then dried under vacuum, the final extraction yielding an extract containing about 5 to about 10% by weight honokiol and about 15 to about 25% by weight magnolol.

Magnolol and honokiol are hydroxybiphenyl compounds, the structures of which being represented as follows:



In the practice of the present invention, the antiplaque efficacy of an oral composition containing a noncationic antiplaque agent such as Triclosan, is synergistically enhanced by the presence in the oral composition of an amount of Magnolia Extract which will yield to the oral composition about 0.001 to about 50% by weight of magnolol and preferably about 0.01 to about 0.3 by weight and about 0.02 to about 0.1% by weight of honokiol and preferably about 0.024 to about 20% by weight.

These amounts of magnolol and honokiol are yielded to the oral composition when the Magnolia Extract about 1 to about 20% by weight of magnolol about 2 to about 50% by weight of honokiol.

Typical examples of noncationic halogenated diphenyl ethers which are particularly desirable from considerations of effectiveness, safety and formulation for use in synergistic combination with the Magnolia Extract are 2,4,4'-trichloro-2-hydroxy-diphenyl ether (Triclosan) and 2,2'-dihydroxy-5,5'-dibromodiphenyl ether.

The synergistic antiplaque combination of Magnolia Extract and noncationic halogenated diphenyl ether may be administered to the oral cavity while dissolved or suspended in a pharmaceutically acceptable vehicle.

When the noncationic halogenated hydroxyphenyl ether is used in combination with Magnolia Extract to prepare oral compositions such as dentifrices and mouthrinses the sassafras, clove, sage, eucalyptus, cinnamon, lemon, and orange, and methyl salicylate. Suitable sweetening agents include sucrose, lactose, maltose, xylitol, sodium cyclamate, perillartine, aspartyl phenyl alanine methyl ester, saccharine and the like. Suitably, flavor and sweetening agents may each or together comprise from about 0.1% to 5% or more of the preparation.

Antitartar agents such as sodium tripolyphosphate, tetrapotassium or tetrasodium pyrophosphate, or mixtures

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thereof, can be present in the oral compositions of the present invention at concentrations from about 0.5 to about 8% by weight.

Agents used to diminish teeth sensitivity such as potassium chloride, potassium nitrate and potassium citrate can also be included in oral compositions of the present invention at concentrations of about 0.1 to about 10% by weight.

Various other materials may be incorporated in oral compositions of this invention including preservatives, such as sodium benzoate, vitamins and chlorophyll compounds. These adjuvants, when present, are incorporated in the compositions in amounts which do not substantially adversely affect the properties and characteristics desired.

The oral compositions of the present invention may be prepared by suitably mixing the ingredients. For instance, in the preparation of a mouthrinse, the noncationic halogenated hydroxyphenyl ether and hydrogenated lupulone antibacterial agent combination is dispersed in a mixture of ingredients, e.g. alcohol, humectants, surfactants, and flavor are then added and mixed. The ingredients are then mixed under vacuum for about 15–30 minutes. The resulting rinse product is then packaged. Dentifrices are prepared similarly, additional thickener and polishing agents being included in the last or penultimate step.

The antiplaque combination of this invention can be incorporated in lozenges, or in chewing gum or other products, e.g. by stirring into a warm gum base or coating the outer surface of a gum base, illustrative of which may be mentioned include jelutone, rubber latex and vinylite resins desirably with conventional plasticizers or softeners, sugar or other sweeteners or carbohydrates such as glucose, sorbitol and the like.

The vehicle or carrier in a tablet or lozenge is a non-cariogenic solid water-soluble polyhydric alcohol (polyol) such as mannitol, xylitol, sorbitol, malitol, a hydrogenated starch hydrolyzate, hydrogenated glucose, hydrogenated disaccharides or hydrogenated polysaccharides, in an amount of about 90 to 98% by weight of the total composition. Salts such as sodium bicarbonate, sodium chloride, potassium bicarbonate or potassium chloride may totally or partially replace the polyol carrier. Tableting lubricants, in minor amounts of about 0.1 to 5% by weight, may be incorporated into the tablet or lozenge formulation to facilitate the preparation of both the tablets and lozenges. Suitable lubricants include vegetable oils such as coconut oil, magnesium stearate, aluminum stearate, talc, starch and Carbowax.

Lozenge formulations contain about 2% gum as a barrier agent to provide a shiny surface as opposed to a tablet which has a smooth finish. Suitable non-cariogenic gums include kappa carrageenan, carboxymethyl cellulose, hydroxyethyl cellulose and the like.

The lozenge or tablet may optionally be coated with a coating material such as waxes, shellac, carboxymethyl cellulose, polyethylene/maleic anhydride copolymer or kappa-carrageenan to further increase the time it takes the tablet or lozenge to dissolve in the mouth. The uncoated tablet or lozenge is slow dissolving, providing a sustained release rate of active ingredients of about 3 to 5 minutes. Accordingly, the solid dose tablet and lozenge composition of this invention affords a relatively longer time period of contact of the teeth in the oral cavity with the active ingredients.

The following Examples further illustrate the present invention, but it is understood that the invention is not limited thereto. All amounts and proportions referred to

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herein and in the appended claims are by weight unless otherwise indicated.

EXAMPLE I

A 0.3% solution in ethanol of Magnolia Extract containing 8% by weight honokiol and 21% by weight magnolol and a 0.3% by weight solution in ethanol of Triclosan were prepared, and the mixed solution at a 1:1 weight ratio designated "Composition 1" was evaluated in an MIC assay for bactericidal activity against *S. mutans* and *F. nucleatum*. The bacterial strain *F. nucleatum* is implicated in the occurrence of gingivitis.

MIC Assay

The bacterial strains of *S. Mutans* and *F. nucleatum* grown for 24 hours in trypticase soy broth and FTG* broth for 48 hours at 37° C. respectively to adjust its optical density between 0.1 and 0.2 absorption units at 610 nm prior to MIC determinations.

The Magnolia Extract and Triclosan solution mixture (Composition 1) was diluted and MIC assayed using the microtiter format according to standard procedures (Manual of Clinical Microbiology, 1995). The results are recorded in Table I below.

The FIC value (fractional inhibitory concentration) of Composition 1 was determined to assess whether the antibacterial efficacy of the Magnolia Extract Triclosan combination exhibited synergistic activity as is described in L. B. Quesnel et al in Journal of Applied Bacteriology, 1978, vol. 45, pages 397-405, L. O. Garrod et al in Antibiotic and Chemotherapy, pages 282-286 and 514-518.

$$FIC = \frac{MIC \text{ of Triclosan in mixture}}{MIC \text{ of Triclosan alone}} +$$

$\frac{MIC \text{ of Magnolia Extract in mixture}}{MIC \text{ of Magnolia Extract alone}}$	FIC	Implies
	<=0.7	Synergism
	1 +/- 0.3	Additive
	>=1.3	Antagonistic

The FIC value for the Magnolia Extract/Triclosan combination is recorded in Table I.

For purposes of comparison, individual 1% by weight solutions of Magnolia Extract, (designated "Composition C1") and Triclosan, (designated "Composition 2") were also subjected to MIC assay. The results are also recorded in Table I below.

TABLE I

Composition No.	Solution	<i>S. mutans</i>	<i>F. nucleatum</i>
C1	Magnolia Extract	62.5 ± 0.0	31.3 ± 0.0
C2	Triclosan	15.6 ± 0.0	2.0 ± 0.0
1	Magnolia Extract + Triclosan FIC Composition 1	7.8 ± 0.0 0.62	1.3 ± 0.6 0.69

The results recorded in Table I show that Composition 1, the combination of the Magnolia Extract and Triclosan exhibit significantly greater bactericidal activity against *S. mutans* and *F. nucleatum* than would be expected from the additive effect of these materials. The FIC value for Composition 1 indicates an unexpected synergistic antibacterial activity against *S. mutans* and *F. nucleatum*.

EXAMPLE II

A dentifrice formulation (designated "Composition A") containing both Triclosan and a Magnolia Extract containing

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8% by weight honokiol and 21% by weight manganol and the ingredients listed in Table II was prepared. A dentifrice having substantially same ingredients as Composition A except that the Magnolia Extract was not included in the dentifrice was used as a comparative composition and designated "Composition B". The ingredients of Compositions A and B are recorded in Table II below.

TABLE II

Composition Ingredients	A Weight %	B Weight %
Di water	16.107	15.807
Glycerin	20.00	20.00
Carboxymethyl cellulose	1.100	1.100
Carrageenan	0.400	0.400
Sodium saccharin	0.300	0.300
Sodium fluoride	0.243	0.243
Titanium dioxide	0.500	0.500
Noncrystallizing sorbitol	20.850	20.850
Gantrez S-97	15.000	15.000
Silica abrasive	20.000	20.000
Silica thickener	1.500	1.500
Flavor	1.000	1.000
Sodium hydroxide - 50% solution	1.200	1.200
Triclosan	0.300	0.300
Magnolia Extract	0	0.300
SLS	1.500	1.500
TOTAL	100.000	100.000

In a six week study to monitor the effect of Composition A and comparative Composition B on gingivitis, 40 subjects were randomly assigned to one of two treatment groups, one group of subjects brushed their teeth twice daily with Composition A and the second group with Composition B. Product efficacy was clinically assessed using standard scoring methods. All subjects were examined professionally at baseline, three and six week intervals for presence of gingivitis according to the Gingival Index system a (G I, Loe 1967).

The scoring criteria was as follows:

Gingivital Inflammation

Score 0 Absence of inflammation

Score 1 Mild inflammation—slight change in color and little change in texture

Score 2 Moderate inflammation—moderate glazing, redness, edema and hypertrophy-bleeding on probing

Score 3 Severe inflammation—marked redness and hypertrophy; tendency to spontaneous bleeding

The GI score results are recorded in Table III as average/tooth/subject score.

TABLE III

		Gingival Index Scores			
		Elapsed Time			% Reduction
Dentifrices	N	Base-line	3 Weeks	6 Weeks	v. Baseline P
Composition A	20	1.09	0.02	0.04	95% P = 0.002
Composition B	20	1.11	0.67	0.58	47%

The results recorded in Table III indicate that the presence of the Magnolia Extract in the dentifrice composition produced a significant reduction in gingivitis by those subjects who brushed their teeth with Composition A.

What is claimed is:

1. An oral antigingivitis composition comprising an orally acceptable vehicle of a combination of a noncationic halogenated hydroxydiphenyl ether and an extract of Magnolia Cortex, the bark of Magnolia officinalis containing hydroxybiphenol compound selected from the group consisting of magnolol, honokiol, and mixtures thereof whereby plaque bacteria growth inhibition from the combination of the halogenated hydroxydiphenyl ether and hydroxybiphenol compounds exceeds the additive effect from the compounds if employed alone, the effective amount of the hydroxydiphenyl ether being in the range of about 0.003 to about 2% by weight and that of the Magnolia Extract being in the range of 0.001 to about 10% by weight, and containing 2 to 50% by weight magnolol and 1 to 20% by weight honokiol.
2. The composition of claim 1 wherein the nonionic halogenated diphenyl ether compound is Triclosan.
3. The composition of claim 1 wherein the hydroxybiphenyl compounds are selected from magnolol, honokiol and mixtures thereof.
4. The composition of claim 1 wherein there is present in the composition a synthetic anionic polycarboxylate.
5. The composition of claim 4 wherein the polycarboxylate is a methyl vinyl ether/maleic anhydride copolymer.
6. A method of inhibiting the growth of plaque bacteria by contacting the bacteria with a composition comprising a pharmaceutically acceptable vehicle and an effective anti-

plaque amount of a combination of a noncationic halogenated hydroxydiphenyl ether and a Magnolia Extract containing hydroxybiphenyl compounds selected from the group consisting of magnolol, honokiol, and mixtures thereof whereby plaque bacteria growth inhibition from the combination of the halogenated hydroxydiphenyl ether and hydroxybiphenol compounds exceeds the additive effect from the compounds if employed alone, the effective amount of the hydroxydiphenyl ether being in the range of about 0.003 to about 2% by weight and that of the Magnolia Extract being in the range of 0.001 to about 10% by weight, and containing 2 to 50% by weight magnolol and 1 to 20% by weight honokiol.

7. The method of claim 6 wherein the nonionic halogenated diphenyl ether compound present in the composition is Triclosan.

8. The method of claim 6 wherein the hydroxybiphenyl compounds of the Magnolia extract present in the composition are selected from magnolol, honokiol and mixtures thereof.

9. The method of claim 6 wherein there is present in the composition a synthetic anionic polycarboxylate.

10. The composition of claim 9 wherein the polycarboxylate is a methyl vinyl ether/maleic anhydride copolymer.

* * * * *

**SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
DIRECCIÓN DE NUEVAS CREACIONES**

2020
Bogotá, D.C.,

/ Abogado: **JUAN PABLO CADENA SARMIENTO**

ASUNTO: Radicación No. 05-58653
Trámite 002
Evento 001
Actuación 430
Oficio
Folios

Nº 15445

Patente de Invención ☒

Vía Nacional ☐

Vía PCT (fase nacional) ☒

Cap. I ☒

Cap. II ☐

No. Solicitud Internacional: PCT/US2005/040568

Fecha de Presentación Internacional: WO2006065403

Como resultado del Examen de Fondo, realizado con fundamento en el artículo 45 de la Decisión 486 de la Comisión de la Comunidad Andina, se comunica:

Documentos estudiados:

Descripción: Folios 34 a 46 como se radicó inicialmente.

Reivindicaciones: Folios 47 a 49 como se radicó inicialmente.

Prioridad: US2004 60635352 (2004-12-10)

US2005 11256789 (2005-10-24)

Objeto de la Invención

Título de la invención: Composición para el cuidado bucal y control del sarro que contienen extracto de magnolia.

Problema Técnico Planteado: Necesidad de composiciones alternativas antiplaca, anti gingivitis y anticálculos con agentes naturales.

Solución: Composición oral con extracto de magnolia y un sistema anticálculo, antiplaca y anti gingivitis.

IPC: A61Q11/00; A61K8/34; A61K8/97; A61K8/24

Excepciones a la Patentabilidad (Art 20 D 486 literales (a) – (d))

Las reivindicaciones 16 a 18 y 20 a 22 se refieren a un método de prevención y tratamiento de la placa y los cálculos de en una superficie bucal. Teniendo en cuenta lo anterior y de acuerdo al artículo 20 D486 los métodos de tratamiento no son patentables por lo cual estas reivindicaciones deben ser retiradas del capítulo reivindicatorio.

Análisis de la Solicitud de Patente

Reivindicaciones (Art 30 D 486, Art 22 PCT)

Las reivindicaciones 1 a 4, 7, 8, 10, 11, 13, 14, 19 y 23 a 27 contienen el término "aproximadamente", dicho término no se acepta pues es impreciso y hace que dichas reivindicaciones dejen de ser clara y concisas, y de igual manera no permite una comparación con el estado de la técnica.

La reivindicación 23 contiene el termino "al menos un" el cual es impreciso y no define de manera concisa la invención ya que al establecer "al menos un compuesto" las posibilidades son amplias. Se debe delimitar el objeto de invención de mejor manera.

Las reivindicaciones 19 y 23 establecen una "cantidad segura y eficaz" de los componentes de la composición. Dicho término no define la invención y esta puede entenderse de varios modos o admitir distintas interpretaciones por lo cual se solicita de finir el objeto de invención de una manera más concisa.

Las reivindicaciones 1, 23 son reivindicaciones que se encuentran como independientes dentro del capítulo reivindicatorio. Sin embargo, dichas reivindicaciones se refieren a una composición de STPP y TSPP cuyas proporciones son iguales (expresadas de diferente manera); por lo cual se solicita que se establezca de manera concreta cual de las dos reivindicaciones define de mejor manera la invención.

La reivindicación 15 establece una composición donde el compuesto activo se extrae por medio de un proceso de extracción; a partir de lo anterior se debe aclarar que las composiciones no se caracterizan por el método de extracción del compuesto activo, por lo cual se debe retirar esta reivindicación del capítulo en cuestión.

Determinación del Estado de la Técnica

El Estado de la Técnica se determinó con base en la fecha de solicitud prioritaria 2004-12-10 y se encontraron los siguientes documentos que anticipan el objeto de esta solicitud:

Item	Documento	Título	Fecha de Publicación
D1	US6500409	<i>Synergistic antiplaque/antigingivitis oral composition</i>	2002-12-31
D2	US5356615	<i>Antiplaque oral compositions</i>	1994-10-18

D1- Una composición oral del cuidado que contiene una combinación sinérgica de antiplaca/antigingivitis de un compuesto difenilhalogenado no iónico tal como Triclosan y un extracto de *magnolia Officinalis* que contiene honokiol y magnolol.

D2- Una composición oral antiplaca, que contiene triclosan como componente principal y sustancia aromática fenólica, tal como eucalpol, timol, salicilato de metilo, mentol, fenol, y/o derivados halogenados que proporciona una acción potencializadora.

Análisis de Patentabilidad (Art 14 D486)

Novedad (Art 16 D486)

Respecto a la solicitud en estudio:

1. La reivindicación 1 dice:

“Una composición oral que comprende:

- (a) Un **compuesto activo de un extracto de magnolia**; y
- (b) Un sistema anticálcico que comprende **pirofosfato de tetrasodio (TSPP)** y **tripolifosfato de sodio (STPP)**, donde dicho TSPP está presente en aproximadamente 0,5 y aproximadamente 2,5%, y dicho STPP está presente en una cantidad de aproximadamente 1 y aproximadamente 10% del peso de la composición”.

Las **características esenciales** de la reivindicación 1 habían sido divulgadas previamente en **D1** ya que divulga una composición para el cuidado oral que comprende:

- a) Un compuesto activo de un extracto de magnolia (magnolol y honokiol) (Columna 2, línea 20 a 23; Columna 3, línea 32 a 36; reivindicaciones 1 y 3); y
- b) Un sistema anticálcico que comprende pirofosfato de tetrasodio (TSPP) (Columna 3, línea 66) y tripolifosfato de sodio (STPP) (Columna 3, línea 67), donde dicho TSPP está presente en aproximadamente 0,5 y aproximadamente 2,5%, y dicho STPP está presente en una cantidad de aproximadamente 1 y aproximadamente 10% del peso de la composición (Columna 2, línea 20 a 23; Columna 3, línea 32 a 36; reivindicaciones 1 y 3).

A partir de lo anterior la reivindicación 1 **no es nueva**.

La reivindicación dependiente 6 reivindica la composición oral donde el policarboxilato aniónico es un **copolímero de anhídrido malénico y metilvinil éter**.

D1 da a conocer que las composiciones orales pueden contener componentes como **policarboxilatos aniónicos** dentro de los que se encuentran **copolímero de anhídrido malénico y metilvinil éter** (Columna 4, línea 54 a 56; reivindicaciones 9 y 10) por lo cual esta reivindicación no es nueva.

2. La reivindicación 19 dice:

“Una composición oral estable eficaz antiplaca, anticalculos y antigingivitis que comprende:

- (a) Una cantidad segura y eficaz de un ingrediente antibacteriano que comprende un **extracto de magnolia** en una concentración de aproximadamente 0.001 y aproximadamente 10% de la composición;
- (b) Una cantidad segura y eficaz de un sistema anticálcico que consiste esencialmente de **pirofosfato de tetrasodio (TSPP)**, **tripolifosfato de sodio (STPP)** y un **copolímero de anhídrido malénico y metilvinil éter**, TSPP está presente en aproximadamente 0,5 y aproximadamente 2,5%, dicho STPP está presente en una cantidad de aproximadamente 1 y aproximadamente 10% y dicho copolímero de anhídrido malénico y metilvinil éter está presente entre aproximadamente 0.5 y aproximadamente 1,5% en base al peso total de la composición; y
- (c) Un **vehículo oralmente aceptable**

Respecto al estado de la Técnica **D1** divulga una composición para el cuidado oral antiplaca y antigingivitis que comprende:

- (a) Una cantidad segura y eficaz de un ingrediente antibacteriano que comprende un extracto de magnolia en una concentración de aproximadamente 0.001 y aproximadamente 10% de la composición Columna 2, línea 20 a 23; Columna 3, línea 32 a 40; reivindicación 1);
- (b) Una cantidad segura y eficaz de un sistema anticálculo que consiste esencialmente de pirofosfato de tetrasodio (TSPP) (Columna 3, línea 66), tripolifosfato de sodio (STPP) (Columna 3, línea 67), y un copolímero de anhídrido malénico y metilvinil éter (Columna 4, línea 54 a 56; Tabla II; reivindicaciones 5, 9 y 10), TSPP está presente en aproximadamente 0,5 y aproximadamente 2,5% (Columna 3, línea 66), dicho STPP está presente en una cantidad de aproximadamente 1 y aproximadamente 10% (Columna 3, línea 67) y dicho copolímero de anhídrido malénico y metilvinil éter está presente entre aproximadamente 0.5 y aproximadamente 1,5% en base al peso total de la composición (Columna 4, línea 54 a 56; Tabla II; reivindicaciones 5, 9 y 10) y
- (c) Un vehículo oralmente aceptable (Columna 4, línea 34 a 40)

A partir de lo anterior las **características esenciales** de la reivindicación 19 habían sido divulgadas previamente en D1, por lo cual la reivindicación **no es nueva**.

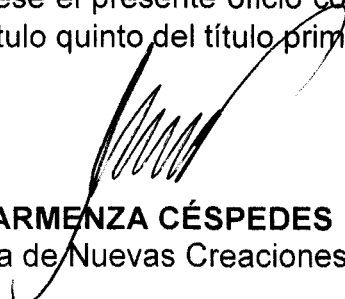
Conclusión

Los requisitos de Patentabilidad de la presente Solicitud se encuentran afectados así:

Nº	Documento	Reivindicaciones afectadas	Requisito que afecta
D1	US6500409	1-27	Novedad

En cumplimiento del artículo 45 de la Decisión 486 de la Comisión de la Comunidad Andina, se le indica que debe dar respuesta dentro del término de 60 días contados a partir de la fecha de notificación de la presente comunicación. En caso de no dar respuesta al presente requerimiento, o si a pesar de la respuesta subsistieran los impedimentos para la concesión, se denegará la patente.

Notifíquese el presente oficio conforme a lo dispuesto en el numeral 5.2, literal e), del capítulo quinto del título primero de la Circular Única N° 10 de 2001.


ALIX CARMENZA CÉSPEDES DE VERGEL
 Directora de Nuevas Creaciones (C)

El anterior requerimiento fue notificado por fijación en lista, de fecha 16 NOV 2010

CONCEPTO TECNICO NUMERO: 3437	EXAMINADOR TÉCNICO Código: 202093
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