



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<p>(51) International Patent Classification⁶ : A61K 7/16</p>	<p>A1</p>	<p>(11) International Publication Number: WO 99/32075</p> <p>(43) International Publication Date: 1 July 1999 (01.07.99)</p>
<p>(21) International Application Number: PCT/US98/25496</p> <p>(22) International Filing Date: 2 December 1998 (02.12.98)</p> <p>(30) Priority Data: 60/068,391 22 December 1997 (22.12.97) US</p> <p>(71) Applicant: WARNER-LAMBERT COMPANY [US/US]; 201 Tabor Road, Morris Plains, NJ 07950 (US).</p> <p>(72) Inventors: PARIKH, Rita, M.; 496 Tether Lane, Paramus, NJ 07652 (US). HARPER, David, Scott; 178 Sycamore Terrace, Glen Rock, NJ 07452 (US). TALWAR, Anil, Kumar; 75 East Mill Road, Long Valley, NJ 07853 (US). KOHUT, Bruce; 126 Cranmoor Drive, Toms River, NJ 08753 (US).</p> <p>(74) Agents: RYAN, M., Andrea; Warner-Lambert Company, 201 Tabor Road, Morris Plains, NJ 07950 (US) et al.</p>		<p>(81) Designated States: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HR, HU, ID, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, UZ, VN, YU, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).</p> <p>Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p>
<p>(54) Title: COMPOSITIONS FOR INHIBITING GINGIVITIS</p> <p>(57) Abstract</p> <p>A stable dentifrice composition containing thymol, eucalyptol, methyl salicylate and menthol is effective in reducing gingivitis.</p>		

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece			TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	NZ	New Zealand		
CM	Cameroon			PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

COMPOSITIONS FOR INHIBITING GINGIVITIS

5

BACKGROUND OF THE INVENTION

1. FIELD OF THE INVENTION

The present invention relates to compositions and a method for inhibiting gingivitis. Specifically, the invention is directed to a dentifrice composition with particular amounts of specific essential oils and a method for treating gingivitis by brushing with the dentifrice composition.

2. DESCRIPTION OF RELATED ART

Volatile or essential oils are widely used in oral care products. Essential oils are aromatic compounds that are derived from plant sources or synthesized. Some essential oils show long-lasting germicidal effectiveness against the most common pathogens in the mouth. These pathogens are frequently associated with oral malodor, plaque and gingivitis. Thymol is a well-known essential oil widely used as an antimicrobial in oral care products. Other essential oils include menthol, methyl salicylate, eucalyptol, anethol and eugenol.

Essential oils have been included in formulations of toothpaste. U.S. Patent No. 1,526,940 to Staegemann teaches a toothpaste with the germicide ammonium ichthyol sulphonate with high amounts of thymol, menthol, eucalyptol, methyl salicylate, and peppermint oil as flavorants and taste-masking ingredients.

U.S. Patent No. 3,164,524 to Fand et al. teaches an oral antiseptic comprising 2, 2'-thiobis-(4,6-dichlorophenol), boric acid, methyl salicylate, thymol, menthol and eucalyptol.

U.S. Patent No. 5,094,843 to Mazzanobile et al. teaches an anti-plaque, anti-gingivitis toothpaste with a fluoride source and an antimicrobial agent consisting essentially of about 0.15% to about 0.80% thymol, about 0.15% to about 1.00% methyl salicylate, about 0.25% to about 0.80% eucalyptol and from about 0.15% to about 0.60% menthol. Mazzanobile et al. teach that the toothpaste will usually have a pH of from about 4 to about 8. The only example in Mazzanobile et al. has a pH of about 6.3. Mazzanobile et al. also disclose that Euthymol toothpaste has been sold in the United Kingdom. According to Mazzanobile et al. Euthymol toothpaste contains 0.12% thymol, 1.26% methyl salicylate, 0.07% menthol and 0.012% eucalyptol. Euthymol toothpaste has a pH of approximately 7.3-7.5.

European Patent Application 0497476 to Colgate-Palmolive Co. teaches an antiplaque oral composition, including a toothpaste, with triclosan. The antiplaque activity of the triclosan is increased by essential oils such as eucalyptol, thymol, methyl salicylate, and menthol.

5 PCT Application WO 96/03109 to Warner-Lambert Company teaches an antiseptic, anticaries dentifrice having a pH of about 3.0 to about 5.5. The dentifrice contains thymol from about 0.01% w/w to about 1.0 % w/w, menthol from about 0.01 w/w to about 1.0% w/w, eucalyptol from about 0.01% w/w to about 1.0% w/w and methyl salicylate from about 0.01% w/w to about 1.0% w/w.

10 Sloane, "Henley's Twentieth Century Book of Formulas, Processes and Trade Secrets" (Gardener D. Hiscox ed., 1965), pp. 252-253 teaches an antiseptic tooth powder containing the antiseptic ingredients of Listerine. The formula contains 20 grains each of thymol, menthol, eucalyptol and oil of wintergreen (methyl salicylate).

15 U.S. Patents Nos. 4,545,979 and 4,550,018 to Ambike et al. teach a dental hygiene composition in an acidic pH range of from 3.0 to 5.0, pH buffers, fluoride, thymol, eucalyptol, methyl salicylate, peppermint and spearmint oil flavors, and 0.1 to 2.0 percent by weight of one or more highly pure alkali metal salts of dodecyl sulphate having less than 5% non-dodecyl alkyl sulphate salts.

Canadian Patent No. 834131 to Tisserand teaches a dentifrice preparation that has an acidic pH of about 3.8 to 5.8, optimally a pH of 4.0 to 5.5, and most preferably a pH of 4.0 to 4.8; fluoride; and contains flavor oils such as menthol, methyl salicylate or thyme oil and other flavors such that the composition is substantially free of hydrocarbon terpenes. According to Tisserand, when essential oils that are not free of terpenes are employed in a fluoride dentifrice that has a pH in the range of about 3.8 to 5.8, the flavor develops a pronounced rancid and sour taste in a period of less than 3 months.

Warner-Lambert has marketed Euthymol® Toothpaste that was formulated with thymol, eucalyptol, methyl salicylate and menthol at a pH above 7.0. This toothpaste was not formulated with fluoride. Warner-Lambert has also marketed Listerine® toothpaste in the United States and Canada that did not contain thymol or eucalyptol and was formulated at a pH above 6.0. This toothpaste did not contain fluoride.

While the prior art discloses toothpaste and other dentifrice compositions with antiseptic essential oils, there is a need for dentifrice compositions providing antigingivitis efficacy. Additionally, there is a need for a dentifrice composition containing antigingivitis ingredients that remain stable for extended periods.

SUMMARY OF THE INVENTION

The present invention is directed to a method of inhibiting gingivitis comprising brushing the oral cavity with a dentifrice composition including about 0.5 % w/w to about 0.7% w/w thymol, about 0.5% w/w to about 0.7% w/w methyl salicylate, about 0.7 % w/w to about 1.0% w/w eucalyptol and about 0.3% to about 0.6% w/w menthol.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

A dentifrice composition used in conjunction with a toothbrush cleans the accessible tooth surfaces. Dentifrice compositions of this invention contain essential oils having antiseptic properties. When the dentifrice also contains one or more fluoride-releasing compound, the composition also has anticaries activity. Dentifrice compositions of this invention also contain, but are not limited to, one or more of the following dentifrice additives: acidifiers, abrasives, surfactants, binders and thickeners, humectants, sweeteners, desensitizing agents, flavors, colors, and preservatives. The dentifrice composition of the invention is acidified to a pH of about 4.0 to about 5.0 by acidifiers including, but not limited to, phosphoric acid, acidic phosphate salts, benzoic acid, and food grade acids (e.g. citric acid, gluconic acid, etc). The preceding active ingredients and additives are combined in a hydrous or anhydrous vehicle to form a solid (i.e. toothpowder), a semi-solid (i.e. paste or gel), or a liquid.

Essential oils are volatile aromatic oils that are synthetic or are derived from plants by distillation, expression or extraction. Essential oils usually carry the odor or flavor of the plant from which they are obtained. In the dentifrice compositions of this invention, antigingivitis activity is provided by essential oils.

5 Some of these essential oils also act as flavoring agents. The essential oils of this invention include, but are not limited to, thymol, menthol, methyl salicylate (wintergreen oil) and eucalyptol. Thymol, also known by the chemical formula 5-methyl 2-(1-methylethyl) phenol, is obtained from the essential oil of Thymus
vulgaris Labiatae and Monarda punctata Labiatae. Thymol is a white crystalline
10 powder with an aromatic odor and taste. Thymol is soluble in organic solvents but only slightly soluble in deionized water.

Menthol is isolated principally from the oil of Mentha arvensis. In its commercial form, menthol is available as L-menthol crystals obtained from a process involving cooling of the oil. Fractional distillation of peppermint oil that
15 usually contains from about 40% to about 65% menthol represents another important source of menthol. Synthetic sources of L-menthol are also available.

Eucalyptol is derived from the eucalyptus tree. Having a camphoraceous odor and cooling taste, this essential oil is often combined with other essential oils such as menthol in confection formulations to impart medicinal
20 effect. Combinations of menthol and eucalyptol are widely used. Particularly

preferred uses of the menthol-eucalyptol combination include, according to the present invention, dentifrices such as toothpastes or dental gels.

Methyl salicylate is the main ingredient in many essential oils, constituting about 99% of oil of wintergreen (Gaultheria procumbens) and sweet
5 birch (Betula lenta). Methyl salicylate, which has a distinctive refreshing aroma, is used widely in mouthwashes, chewing gums and other oral and pharmaceutical preparations.

The four essential oils used in the present invention are also used in the well known mouthwash Listerine®. The amount of the oils in Listerine®
10 mouthwash is 0.064% thymol, 0.092% eucalyptol, 0.060% methyl salicylate and 0.042% menthol. Listerine® mouthwash is known to help reduce the incidence of gingivitis. The inventors were faced with the challenge of formulating a toothpaste that delivers the same amount of essential oils so as to provide anti-gingivitis activity.

15 The recommended amount of mouthwash used at one time is approximately 20 milliliters. In contrast, the average amount of toothpaste is only approximately 2.0 grams. Based upon the difference in amounts of product used, the inventors believed that a toothpaste with ten times the concentration of essential oils in the mouthwash would be needed to deliver anti-gingivitis activity.

Suprisingly, a dentifrice with only eight times the concentration of essential oils present in Listerine® mouthwash is sufficient to provide anti-gingivitis activity. Specifically, a dentifrice with about 0.46% to about 0.5623% thymol, about 0.4644% to about 0.5676% methyl salicylate, about 0.306% to about 0.374% menthol and about 0.6971% to about 0.8519% eucalyptol is clinically effective in inhibiting gingivitis. More preferably a dentifrice according to the present invention contains about 0.5112% thymol, about 0.5160% methyl salicylate, about 0.34% menthol and about 0.7745% eucalyptol and is clinically effective in inhibiting gingivitis.

Fluoride-releasing compounds may be used in the dentifrice compositions of the present invention. These compounds may be fully or slightly water soluble, release fluoride ions or fluoride-containing ions in water and do not react with other components in the composition. It is well known that dentifrice compositions containing fluoride-releasing compounds help prevent dental caries. Typical fluoride-releasing compounds are inorganic fluoride salts such as water-soluble alkaline earth metal, alkali metal, and heavy metal salts. Sodium monofluorophosphate, sodium fluoride, stannous fluoride and mixtures of these compositions are preferred.

The amount of fluoride-releasing compound present in the dentifrice compositions of this invention must be nontoxic. The specific amount depends upon the type of fluoride-releasing compound employed, the solubility of the

fluoride-releasing compound and the formulation of the dentifrice composition. In general, the fluoride-releasing compound will be present in an amount by weight of up to about 1.2% w/w, preferably from about 0.1% w/w to about 1.0% w/w, and most preferably from about 0.175% w/w to about 0.8% w/w of the dentifrice composition so as to provide 800 - 1500 ppm F⁻.

The pH for the preferred embodiment according to the present invention is from about 4.0 to about 5.0. A pH greater than about 5.0 has been found to decrease the antiseptic activity of the dentifrice composition.

In addition to providing improved antiseptic activity, maintaining the pH of the dentifrice compositions from about 4.0 to about 5.0 also provides for a stable product. The amount of methyl salicylate in the composition drops dramatically over time at a pH greater than 5.0.

The pH of the claimed dentifrice is adjusted to below 5.0 using suitable food or pharmaceutical grade acidifiers. These include, but are not limited to, one or a combination of the following: phosphoric acid, benzoic acid, citric acid, or other tricarboxylic acids, and the like. Acidifiers in the present invention include a mixture of phosphoric acid from about 0.01% w/w to about 3.0% w/w, preferably in the range of from about 0.1% w/w to about 1.5% w/w, and most preferably in the range of from about 0.2% w/w to about 0.75% w/w; monobasic sodium phosphate from about 0.01% w/w to about 1% w/w, preferably from about 0.1% w/w to about 0.5% w/w and most preferably from about 0.2% w/w to about

0.4% w/w; dibasic sodium phosphate from about 0.001% w/w to about 1.0% w/w, preferably from about 0.01% w/w to about 0.5% w/w and most preferably from about 0.01% w/w to about 0.05% w/w; and benzoic acid in the range of from about 0.01% w/w to about 1.0% w/w, preferably from about 0.05% w/w to about 0.5% w/w, and most preferably from about 0.08% w/w to about 0.35% w/w. The exact amount of acidifier added will depend on the final pH and buffer capacity desired.

The pH of the products may be buffered with salts of the acids in question. Common buffer systems include phosphoric acid and sodium phosphate salts, or citric acid and sodium citrate. Suitable buffers for use in this invention include citric acid-sodium citrate, phosphoric acid-sodium phosphate, sodium monobasic phosphate-sodium dibasic phosphate, acetic acid-sodium acetate, gluconic acid-sodium gluconate and benzoic acid and sodium benzoate in amounts up to about 1% w/w, preferably from about 0.05% w/w to about 0.75% w/w of the composition and most preferably from about 0.1% w/w to about 0.5% w/w of the composition.

The compositions of the present invention may also contain conventional dentifrice additives including, but not limited to, humectants, binders, thickeners, surfactants, preservatives, sweeteners, flavors, colors, glycerin, and a buffer. These additives are present in amounts that do not interfere

with the antiseptic, antigingivitis and anticaries properties of the composition of the present invention.

Surfactants or surface active agents are organic compounds that reduce surface tension between liquids and aid in the dispersion of a composition throughout the oral cavity. The surfactant in the present invention may be anionic, nonionic, or amphoteric. The oral hygiene or dentifrice compositions of the present invention may contain surfactants in amounts up to about 5.0% w/w; preferably from about 0.1% w/w to about 3.0% w/w of the dentifrice composition; and most preferably from about 0.2% w/w to about 2.0% w/w of the dentifrice composition.

The most preferred surfactants are anionic. These anionic surfactants include, but are not limited to, sodium lauryl sulfate, sodium lauroyl sarcosinate, sodium methyl cocoyl taurate, and disodium lauryl sulfosuccinate. A preferred surfactant is sodium lauryl sulfate. The compositions according to the present invention are substantially free from one or more highly pure alkali metal salts of dodecyl sulphate having less than 5% non-dodecyl alkyl sulphate salts.

Amphoteric surfactants have the capacity to behave as either an acid or a base and include quaternized imidazole derivatives. Preferred amphoteric surfactants include long chain (alkyl) amino-alkylene alkylated amine derivatives, also known as MIRANOL®, manufactured by Rhone-Poulanc, Cranberry, New Jersey.

Natural and artificial sweeteners may be used in the dentifrice compositions. The sweetener may be selected from a wide range of well known materials including naturally occurring water-soluble sweeteners, artificial water-soluble sweeteners and modified water-soluble sweeteners derived from naturally occurring water-soluble sweeteners. Artificial water-soluble sweeteners include, but are not limited to, soluble saccharin salts, e.g., sodium or calcium saccharin salts, cyclamate salts, the sodium, ammonium or calcium salt of 3,4-dihydro-6-methyl-1,2,3-oxathiazine-4-one-2,2-dioxide, the potassium salt of 3,4-dihydro-6-methyl-1,2,3-oxathiazine-4-one-2,2-dioxide (Acesulfame-K), the free acid form of saccharin and dipeptide based sweeteners, such as L-aspartic acid derived sweeteners. Dipeptide sweeteners include L-aspartyl-L-phenylalanine methyl ester (Aspartame) and materials described in U.S. Pat. No. 3,492,131, L-alpha-aspartyl-N-(2,2,4,4-tetramethyl-3-thietanyl)-D-alaninamide hydrate (Alitame), methyl esters of L-aspartyl-L-phenylglycerine and L-aspartyl-L-2,5-dihydrophenylglycine, L-aspartyl-2,5-dihydro-L-phenylalanine and L-aspartyl-L-(1-cyclohexene)-alanine. Naturally occurring water-soluble sweeteners include, but are not limited to, sugar alcohols, including sorbitol as 70% sorbitol solution, mannitol, xylitol, maltitol, hydrogenated starch hydrolysates and mixtures thereof.

Water-soluble sweeteners derived from naturally occurring water-soluble sweeteners include, but are not limited to, chlorinated derivatives of

The amount of flavor is normally a matter of preference subject to the type of final dentifrice composition, the individual flavor employed and the strength of flavor desired. The flavors are preferably utilized in amounts that may range from about 0.01% w/w to about 6% w/w of the dentifrice composition. The
5 flavors used in the compositions according to the present invention comprise flavoring oils that are not substantially free of terpenes.

Coloring agents are used in amounts effective to produce a dentifrice of the desired color. These coloring agents may be incorporated in amounts up to about 3% by weight of the dentifrice composition. The coloring agents may also
10 include natural food colors and dyes suitable for food, drug and cosmetic applications. These coloring agents are known as FD & C dyes and lakes. The coloring materials are preferably water-soluble. Illustrative nonlimiting examples include the indigoid dye known as FD & C Blue No.1, and D & C Yellow No. 10. A full recitation of all FD & C colorants and their corresponding chemical
15 structures may be found in the Kirk-Othmer Encyclopedia of Chemical Technology, 3rd Edition, in volume 5 at pages 857-884. A preferred opacifier, titanium dioxide, may be incorporated in amounts up to about 2.0% w/w, preferably less than about 1.0% w/w of the composition and most preferably less than about 0.4% w/w.

20 Suitable humectants in this invention include sorbitol, as 70% sorbitol solution, glycerin, propylene glycol, polyethylene glycol, mixtures thereof, and the

like. Humectants may be present in amounts from about 1.0% to about 75.0% by weight of the dentifrice composition.

Suitable abrasive substances for use in this invention must be compatible with the low pH of the composition and include hydrated silica, alumina or alkali metal meta-phosphates. Silica abrasives in the dentifrice composition according to this invention may include among others, ZEODENT® (113), manufactured by J. M. Huber Corp. and SYLOID® or SYLODENT®, manufactured by W.R. Grace Co. These polishing agents may be used in amounts up to about 75.0% w/w of the composition, preferably in amounts from about 5.0% w/w to about 40% w/w of the composition and most preferably from about 5.0% w/w to about 30.0% w/w of the composition.

The dentifrice composition includes an oral vehicle that can be a paste, gel, powder or liquid. Depending upon the specific form of the dentifrice, the composition may also include binders or gelling agents to provide a desired consistency. Gelling agents such as hydroxyethyl cellulose, carboxymethyl cellulose, methyl cellulose, xanthan gum, gelling silicas and the like may be used singly or in combination. The preferred gelling system is a mixture of carboxy methyl cellulose, xanthan gum and gelling silica. Gelling agents may be used in amounts from about 0.5% w/w to about 30% w/w, preferably from about 5.0% w/w to about 15.0% w/w of the dentifrice composition, and most preferably from about 7.0% w/w to about 20% w/w of the composition.

The dentifrice composition of this invention may also contain a desensitizing agent such as strontium chloride, potassium nitrate or sodium citrate-citric acid, which may be used in an amount from about 0.5% w/w to about 10% w/w.

5 Suitable preservatives include benzoic acid, butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), ascorbic acid, methyl paraben, propyl paraben, tocopherols and mixtures thereof. Preservatives when used are generally present in amounts up to about 1.0% w/w, and preferably from about 0.1% w/w to about 1.0% w/w of the dental gel composition.

10 The present invention is further illustrated by the following non-limiting examples. All parts and percentages in the examples and throughout the specification and claims are by weight of the final composition unless otherwise specified.

Example 1 and Comparative Example 1

Dentifrice compositions were formulated with the ingredients listed in Table 1.

5

Table 1.

FORMULA NUMBER	1	Comparative Example 1
PH	4.5	4.5
THYMOL	0.5112	0
METHYL SALICYLATE	0.5160	0
MENTHOL	0.3400	0
EUCALYPTOL	0.7745	0
GLYCERIN	6.0000	6.0000
SORBITOL SOLUTION (70%)	40.0000	40.0000
WATER	25.0820	27.8237
PEG 1450	3.0000	3.0000
XANTHAN GUM	0.2500	0.2500
Na CMC	1.2000	1.2000
FLAVOR	0.2250	0.2250
SODIUM FLUORIDE	0.2540	0.2540
Na SACCHARIN	1.2000	0.6000
NaH ₂ PO ₄	0.2900	0.2900
Na ₂ HPO ₄	0.0300	0.0300
BENZOIC ACID	0.1500	0.1500
TiO ₂	0.3500	0.3500
GELLING SILICA	11.000	11.000
ABRASIVE SILICA	7.0000	7.0000
SLS	1.5000	1.5000
COLOR	0.0022	0.0022

Example 2

A three week, randomized, double blind study was performed studying the antiplaque and antigingivitis efficacy of brushing with Example 1 versus Comparative Example 1. Forty four subjects were screened for evidence of gingivitis and plaque. Subjects were instructed to brush twice daily by filling the head of their toothbrush with the assigned toothpaste and brushing for one minute. The subjects were instructed to not use any other toothpaste or mouthwash during the study.

The subjects were then screened for Modified Gingival Index, Plaque Index and Bleeding Index. The Modified Gingival Index is described in Lobene, R.R., et al., A Modified Gingival Index For The Use In Clinical Trials, Clin. Prev. Dent. 8:3, 1986. The severity of gingivitis is scored using a 4 point scale 0 - normal, 1 mild inflammation in any portion of the unit, 2 - mild inflammation in the entire unit, 3- moderate inflammation, 4 - severe inflammation.

The plaque index used was the Turesky modification of the Quigley-Hein Plaque Index as described in Turesky, S., et al., Reduced Plaque Formation By The Chloromethyl Analogue of Vitamin C, J. Periodontol. 41:41, 1970. This index scores the amount of the toothsurface covered with plaque using a 0-5 point scale.

The bleeding index used was the Gingival Bleeding Index as described in Saxton, et al., The Effect Of A Dentifrice Containing Zinc Citrate And Triclosan On Developing Gingivitis, J. Perio. Res. 24:75, 1989. The level of bleeding is recorded following probing the gingiva with a periodontal probe in a sweeping fashion and using a 3 point scale 0 no bleeding, 1 - bleeding after 30 seconds, and 3 - bleeding immediately.

The subjects using Example 1 had a 39.6% reduction in Plaque Index, a 10.8% reduction in Gingival Index and a 65.4% reduction in Bleeding Index compared to the subjects using Comparative Example 1.

Example 3

A six month study testing Example 1 versus Comparative Example 1 was performed. The procedures and indices used in Example 2 were also used in Example 3. In addition to the indices measured in the three week study, the subjects were also measured for interproximal Modified Gingival Index and interproximal Plaque Index. The subjects were measured at three and six months. The results are summarized in Table 2.

Table 2

	Comparative Example 1	Example 1	
	Adjusted Mean	Adjusted Mean	% Reduction vs. Comparative Example 1
Month 6	(N=154)	(N-158)	
Mean Modified Gingival Index	2.01	1.48	26.2%
Mean Bleeding Index	0.115	0.037	67.7%
Mean Plaque Index	2.45	1.41	42.4%
Mean Int. Mod. Gingival Index	2.23	1.73	22.3%
Mean Int. Plaque Index	2.58	1.58	38.9%
Month 3	(N-155)	(N-161)	
Mean Modified Gingival Index	2.03	1.80	11.6%
Mean Bleeding Index	0.112	0.064	48.8%
Mean Plaque Index	2.67	1.94	27.4%
Mean Int. Mod. Gingival Index	2.21	2.03	8.3%
Mean Int. Plaque Index	2.83	2.16	23.9%

While the invention has been described in detail and with reference to specific examples thereof, it will be apparent to one skilled in the art that various changes and modifications can be made therein without departing from the spirit and scope thereof.

What is claimed is:

1. A dentifrice composition comprising:
about 0.46% to about 0.5623% thymol,
about 0.4644% to about 0.5676% methyl salicylate,
about 0.306% to about 0.374% menthol,
about 0.6971% to about 0.8519% eucalyptol; and
a dental vehicle.
2. The dentifrice composition according to claim 1, comprising:
about 0.5112% thymol,
about 0.5160% methyl salicylate,
about 0.3400% menthol, and
about 0.7745% eucalyptol.
3. A method of inhibiting gingivitis in an oral cavity comprising
brushing the teeth within the oral cavity with a dentifrice composition comprising:
about 0.46% to about 0.5623% thymol,
about 0.4644% to about 0.5676% methyl salicylate,
about 0.306% to about 0.374% menthol,
about 0.6971% to about 0.8519% eucalyptol; and
a dental vehicle.
4. The method according to claim 3, wherein the dentifrice

composition comprises:

about 0.5112% thymol,

about 0.5160% methyl salicylate,

about 0.3400% menthol, and

about 0.7745% eucalyptol.