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3,644,613

**ORAL, NASAL AND LABIAL COMPOSITIONS
CONTAINING MENTHYL KETO ESTERS**

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6 Claims

ABSTRACT OF THE DISCLOSURE

Compositions for application to the oral and nasal areas of the body are disclosed which contain alpha, beta, gamma, delta, epsilon, zeta and eta keto esters of menthol. These compositions impart a long-lasting cooling sensation to tissues of the lips and the mucous membranes of the oral cavity and nasal passages.

This invention relates to improved compositions for use in the oral and nasal areas of the human body. More particularly, this invention relates to compositions which, in their intended mode of usage, come into contact with the nasal passages, the oral cavity, throat and/or the lips, and which contain certain keto esters of menthol to impart a cooling sensation to the tissues of these areas. Such compositions include, but are not limited to nasal drops, sprays and inhalants, cough drops, cough syrups, soothing agents for the throat, lipsticks, lip pomades, mouthwashes, mouthsprays and dentifrices.

The cooling sensation evoked by various aromatic substances is generally considered pleasant and desirable in and around the oral and nasal areas of the body. Consequently, many products which come into contact with these areas contain such "cooling" ingredients. The most commonly used ingredient for imparting this sensation has been menthol. However, there are certain disadvantages in using menthol for this purpose. Firstly, the presence of menthol in a product severely limits the formulator's choice of odor and/or flavoring for the product. This is because menthol has a distinctive minty odor and flavour and an immediate and relatively harsh impact on the mucous membranes of the mouth, nose and throat and on the sensitive areas of chapped lips. Secondly, the cooling sensation of menthol while intense on first application, wastes away rapidly with time. In an endeavour to extend the life of the cooling sensation, the only recourse in the past has been to increase the level of menthol in the product. The relatively large quantity of menthol required to prolong the cooling sensation significantly can irritate the mucous membranes any cause of burning sensation. Because the sensitivity of tactile senses differs so much from person to person, a suitable balance of the two effects has been difficult to attain.

The utilization of menthyl keto esters as additives for smoking tobacco products is described by Jarboe U.S. Pat. 3,136,319, issued June 9, 1964. The sole basis for the inclusion of such materials into *smoking* tobacco products is for the desired benefit "whereby the harshness associated with the *smoke* of a tobacco product is substantially eliminated." Moreover, it is stated that "... the additive or its desirable menthol component is released into the *smoke* stream on smoking the tobacco product at a satisfactorily regulated rate."

It is clear from the teaching of the aforementioned Jarboe patent that the desired result is attained only when these compounds are subjected to the high temperatures of burning tobacco. It is quite apparent therefore that the long-lasting cooling effect disclosed herein which derives from direct contact with the tissues of

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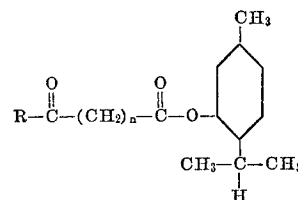
the mucous membranes of the oral cavity and throat and nasal passages at ambient temperatures is not suggested to one skilled in the art.

It is the object of this invention to provide improved organoleptic compositions for application to the oral, throat and nasal areas of the human body.

It is a further object of this invention to provide compositions which impart a long-lasting cooling effect upon contact with the tissues of the nasal, oral and throat areas.

It is still a further object of this invention to provide compositions which impart a long-lasting cooling effect without a strong minty odor and taste or irritating effect.

It has been found that these objectives can be achieved by oral, nasal or labial compositions as hereinafter defined comprising (1) from about 0.01% to about 2.0% by weight of a menthyl keto ester of the formula:



wherein R is an organic radical such as alkyl (e.g. methyl, ethyl, propyl or butyl), aryl (e.g., phenyl or naphthyl) or aralkyl, (e.g., benzyl), and *n* is an integer from 0 to 6; and (2) a carrier suitable for use in the oral cavity, e.g., an oily solvent or emulsion suitable for use on mucous membranes, or a solid wax base. The menthol from which the above-described esters are derived can be 1-menthol and its isomers. Examples of such preferred esters of menthol are menthyl pyruvate, menthyl acetoacetate, menthyl levulinate, menthyl gamma acetyl butyrate and menthyl benzoylacetate. A procedure for preparing menthyl keto esters is described in Journal of the American Chemical Society, vol. 73, pp. 4195-7. Other esters of menthol which can be employed herein include the following: menthyl α -ketobutyrate, menthyl α -ketovalerate, menthyl β -ketovalerate, menthyl phenylpyruvate, menthyl γ -ketocaproate, menthyl delta valerylvalerate, methyl epsilon naphthoyl-caproate and menthyl zeta phenylacetyl enanthylate.

These compositions produce a persistent cooling effect when applied to the lips and membranes of the throat, oral and nasal cavities. In contrast to compositions containing menthol, this long-lasting cooling sensation on the lips and throat, oral and nasal membranes is achieved without irritation of these sensitive areas. Moreover, menthyl keto esters do not have a strong minty odor or taste. Therefore, unlike menthol, they can be used as flavorant additives in compositions in which a non-minty odor or taste is desired.

The menthyl keto esters can be used at levels between 0.01% and 2.0% and preferably at levels between 0.05% and 1.5% by weight in the compositions of this invention. Less than 0.01% will give practically no cooling effect, while more than 2.0% is likely to give an unpleasant taste. Within the aforementioned range, the level of menthyl keto ester chosen for use in a given product will depend on the intensity of cooling effect desired and on the mode of usage of the product. For example, a single usage portion of undiluted mouthwash is about 15 grams compared to a single usage portion of about one gram for a toothpaste. To impart the same cooling effect, therefore, it is necessary to use much more menthyl keto ester in a toothpaste than in a mouthwash.

Although it is to be understood that the flavor portions of the compositions to be described hereinafter can consist entirely of the menthyl keto esters, these esters are actually relatively flavorless and therefore it is preferable to include conventional flavoring substances in the flavoring portions of said compositions.

The compositions of this invention can be classified as oral, nasal or labial. The term oral compositions, as used herein, refers to all products which, in the ordinary course of usage come into contact with the membranes of the oral cavity and throat, that is, products which are applied to, or ingested through the oral cavity. Such products include dentifrices, mouthwashes and mouth-sprays, chewing gums, confections, including medicated confections such as cough drops, cough syrups and lozenges and coatings encapsulating such products; and cough syrups and gum soothing agents.

Dentifrices typically contain an abrasive polishing material, sudsing agents, flavoring and sweetening agents. Toothpastes usually additionally contain humectants and binders.

Any abrasive polishing material which does not excessively abrade dentin can be used in dentifrice compositions. These include, for example, calcium carbonate, dicalcium orthophosphate dihydrate, calcium pyrophosphate, calcium polymetaphosphate, insoluble sodium polymetaphosphate and resinous abrasive materials such as particulate condensation products of urea and formaldehyde and others disclosed by Cooley et al. in U.S. Pat. 3,070,510, granted Dec. 25, 1962.

The total amount of abrasive materials in the dentifrice embodiments of this invention can range from 0.5% to 95% by weight of the dentifrice. (All percentages specified hereinafter refer to weight percent of the total composition unless otherwise specified.) Preferably, toothpastes contain from 20% to 60%, and toothpowders contain from 6% to 95%.

Dentifrices usually contain sudsing agents. Suitable sudsing agents for use in the dentifrices of this invention are those which yield substantial levels of foam and which are otherwise acceptable for use in the oral cavity. Examples of suitable sudsing agents include the water-soluble salts of alkyl sulfate having from 10 to 18 carbon atoms, e.g., sodium coconut monoglyceride sulfonate; water-soluble salts of fatty acid amides of taurine, e.g., sodium N-methyl - N - palmitoyl tauride; water-soluble salts of fatty acid esters of isethionic acid, e.g., the coconut acid ester of sodium isethionate; and substantially saturated aliphatic acyl amides of saturated aliphatic monoaminocarboxylic acid having 2 to 6 carbon atoms and in which the acyl radical contains 12 to 16 carbon atoms, e.g., sodium N-lauroyl sarcosinate. Mixtures of two or more sudsing agents can also be used.

The sudsing agent can be employed at levels ranging from about 0.5% to 5.0%.

Suitable flavoring agents for use in the dentifrices herein include, for example, wintergreen oil (methyl salicylate), oil of peppermint, oil of sassafras (synthetic), and oil of anise. Flavoring agents are present at a level of from 0.01% to 2.0%. Sweetening agents include, for example, saccharin, dextrose, levulose, and sodium cyclamate.

In toothpastes it is desirable to employ thickening agents such as hydroxyethylcellulose and water-soluble salts of cellulose ethers, including sodium carboxymethyl cellulose and sodium carboxymethylhydroxyethyl cellulose; or natural gums, including gum karaya, gum arabic and gum tragacanth. Also, colloidal magnesium aluminum silicate or finely divided silica can be used as part of the thickening agent to improve the texture of the product. Thickening agents in an amount of from 0.1% to 5.0% can be used.

It is also desirable to include some humectant or viscosity modifying material in toothpastes. Suitable materials for these purposes include glycerine, sorbitol, and

other edible polyhydric alcohols or mixtures thereof. These materials can comprise up to 40% of the toothpaste composition. In addition to the aforementioned typical components of a toothpaste, water is normally present in toothpastes at levels up to 50%.

Mouthwashes generally comprise a water/ethyl alcohol solution and about 0.01% to about 2.0% of flavoring materials such as those mentioned above for dentifrices. The alcohol provides an antibacterial effect and also solubilizes the flavoring materials. Optionally, mouthwashes also contain additional antibacterial agents such as cetyl trimethylammonium chloride, sudsing and sweetening agents such as those mentioned above for dentifrices, and humectants such as glycerine and sorbitol which give a moist feel in the mouth.

Typically, mouthwashes contain 10% to 60% ethyl alcohol, 30% to 90% water, 5% to 20% glycerine or other humectant, 0.1% to 2% sudsing agent, 0.05% to 0.5% sweetening agent such as saccharin and 0.05% to 0.3% flavoring agent.

These aforesaid mouthwash compositions can also be administered in vaporizer or aerosol forms. When administered in aerosol form, commonly available propellants such as hydrocarbons and fluoro-halogen derivatives, for example, dichlorodifluoromethane and tetrafluorodichloroethane are used.

Chewing gum comprises a gum base and flavoring materials such as those mentioned above for dentifrices. The flavoring materials are present at a level of 0.01% to about 2.0% of the final chewing gum composition. The gum base is a chewable plastic gum material such as natural rubber, chicle, polyvinyl acetate, ester gum, coumarone resin, and paraffin wax. The gum base is typically made from a mixture of two or more plastic gum materials to achieve a preferred degree of plasticity for chewing. Optionally, corn syrup is added as a softener and binder for the chewing gum and sugar is optionally added as a filler and sweetener. Typical chewing gum compositions comprise 20% to 30% gum base, 15% to 20% corn syrup, 50% to 65% sugar and 0.05% to 1.5% flavoring materials.

Confections comprise a sugar base and one or more flavoring materials. The flavoring materials are present at levels between 0.01% and 2.0%. Optionally, confections can contain various other materials in order to provide confectionary compositions having a wide variety of physical characteristics. Examples of these optional materials include water, syrups such as corn syrup, starches such as cornstarch, vegetable fats and oils such as cocoa butter and coconut oil, and binders such as gum acacia.

A typical confection is a hard candy comprised of a hard candy base and 0.05% to 1.5% flavor. The hard candy base is a solidified solution of amorphous sugar which is generally formed from a sugar solution which has been cooked at high temperature so as to remove nearly all of the moisture. The flavoring materials are added before the moisture is removed. The flavoring materials mentioned hereinbefore for dentifrices are also exemplary of those suitable for use in confections. For confections such as cough drops, cough syrups and throat lozenges medicaments such as antibacterials (e.g. cetyl pyridinium chloride) or antitussives (e.g. diphenhydramine hydrochloride) are often included in the composition.

Those oral composition ingredients other than medicaments and the keto esters of menthol recited in the foregoing disclosure are exemplary of carriers suitable for use in the oral cavity.

The term nasal compositions, as used herein, refers to products which, in the ordinary course of usage, are applied to the nasal passages. Such compositions can comprise an oil-in-water or water-in-oil emulsion or an oily solvent base suitable for use on the mucous membranes such as light mineral oil, vegetable oils, and fatty acid esters, and one or more aromatic chemicals which are solu-

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ble in the base such as camphor, thymol, pine oil, eucalyptol and menthol. These aromatic chemicals are present in the oily solvent base or in the emulsion at levels between 0.01% and 2.0%. When comprised of these basic components, the compositions are liquid including liquids of varying viscosities, and are applied to the nasal cavity in the form of drops, sprays or jellies.

If it is desired to apply them in the form of a solid, such as nose stick, one or more waxes such as white wax or spermacetic is included in the composition at levels from about 20% to about 80%. This gives a soft waxy composition which holds a rigid shape but which leaves a deposit when rubbed against the warm membranes of the nasal cavity. Nasal compositions can also optionally contain pharmacologically active ingredients e.g., a bronchial muscle relaxant such as amphetamine.

The term labial compositions, as used herein, refers to products which, in the ordinary course of usage are applied to the lips. These include lipsticks, lip pomades and lip creams. These products comprise one or more oils such as castor oil and mineral oil, one or more waxes such as beeswax, paraffin, carnauba or ceresin wax and aromatic chemicals for flavor and/or odor effects. The oil is present in these compositions at levels between 25% and 65%, the wax is present at levels between 30% and 70% and the aromatic chemicals are present at levels between 0.01% and 2.0%. The aromatic chemicals can be flavoring oils such as those mentioned hereinbefore for dentifrices or they can be the types more commonly used in cosmetics such as rose oil, rhodinol, methyl ionone or Peru balsam. Optionally, coloring materials can also be added to labial compositions to impart a color to the lips. Suitable coloring ingredients are those approved by the U.S. Food and Drug Administration for use in cosmetics likely to come into contact with the mouth, such as D & C Red No. 1 and D & C Orange No. 1. When coloring materials are present, they are used at levels up to about 3% of the finished composition.

The following examples are given solely for the purpose of illustration and are not to be construed as limitations of this invention, many variations of which are possible without departing from the spirit or scope thereof.

EXAMPLE I

Toothpaste compositions are prepared according to the following formulas, having menthol present in one and a molar equivalent amount of menthyl keto ester in the other.

	Parts by weight	
	A	B
Dicalcium orthophosphate dihydrate.....	44.00	44.00
Sorbitol (30% aqueous solution).....	6.25	6.25
Glycerine.....	18.00	18.00
Hydroxyethylcellulose.....	2.00	2.00
Sodium lauryl sulfate.....	0.37	0.37
Sodium coconut monoglyceride sulfonate.....	0.75	0.75
Magnesium aluminum silicate.....	0.40	0.40
Saccharin.....	0.12	0.12
Coloring.....	0.47	0.47
Flavoring:		
Methyl salicylate (wintergreen oil).....	0.60	0.60
Menthol.....	0.30	0.30
Menthyl acetoacetate.....		0.45
Water.....		Balance to 100

When one brushes the teeth with Formula A he experiences a minty-wintergreen flavor and a cooling sensation which remains in the mouth for a relatively short time after brushing. When one brushes the teeth with Formula B, a representative oral composition of this invention, one experiences a wintergreen flavor with no minty overtones, and a cooling sensation which persists in the mouth much longer than the cooling sensation imparted by Formula A. Substantially equivalent results are secured when menthyl pyruvate, menthyl levulinate, menthyl γ -acetyl butyrate or menthyl benzoylacetate are used in Formula B in the place of menthyl acetoacetate.

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EXAMPLE II

A mouthwash in accordance with this invention is formulated as follows:

	Parts by weight
5 Ethyl alcohol (50% in H ₂ O)	81.00
Glycerine	12.00
Saccharin	0.30
Flavoring:	
Methyl salicylate	0.10
Menthyl levulinate	0.15
Sodium coconut monoglyceride sulfonate	0.6
Water	Balance to 100

This mouthwash, when used in the normal way, provides a wintergreen flavor with no minty overtones, and a long-lasting cooling sensation in the mouth. Similar results are achieved when the menthyl levulinate of this example is replaced by an equivalent amount of menthyl α -keto-butyrate, menthyl α -ketovalerate, menthyl β -ketovalerate, menthylphenylpyruvate, menthyl γ -ketocaproate, menthyl delta valeryl-valerate, menthyl epsilon naphthoyle caproate or menthyl zeta phenylacetyl enanthylate.

A mouthwash composition in aerosol form is prepared having the following ingredients:

	Parts by weight
25 Ethyl alcohol	50.00
Glycerine	4.70
Saccharin	0.30
30 Flavoring:	
Methyl salicylate	3.0
Menthyl levulinate	2.0
Propellant: dichlorodifluoromethane	40.0

This mouthwash, in aerosol form, when used in the normal fashion, provides a wintergreen flavor with no minty overtones, and a longlasting cooling sensation in the mouth.

EXAMPLE III

A chewing gum in accordance with this invention is formulated as follows:

	Parts by weight
45 Gum base	21.30
Ester gum	6.40
Coumarone resin	9.60
Dry latex rubber	3.20
Paraffin wax (M.P. 180° F.)	2.10
Sugar	59.75
50 Corn syrup (Baumé 45)	18.20
Flavoring:	
Methyl salicylate	0.60
Menthyl gamma acetyl butyrate	0.45

This chewing gum, when used in the usual manner, imparts to the mouth a wintergreen flavor with no minty overtones, and a long-lasting cooling sensation.

EXAMPLE IV

A throat lozenge is formulated in the following manner:

	Parts by weight
65 Hard candy base	93.70
Cetyl pyridinium chloride	0.30
Flavoring:	
Methyl salicylate	0.10
Menthyl acetoacetate	0.90

This throat lozenge, when used in the normal manner, kills bacteria in the mouth and throat, gives a pleasing wintergreen flavor with no minty overtones, and imparts a cooling sensation to the membranes of the mouth and throat which persists for a considerable length of time after the lozenge has been dissolved and ingested.

UNITED STATES PATENT OFFICE
CERTIFICATE OF CORRECTION

Patent No. 3,644,613 Dated February 22, 1972

Inventor(s) Alfred H. Moeller, Michel Demont and Albert G. Nickstad

It is certified that error appears in the above-identified patent and that said Letters Patent are hereby corrected as shown below:

Column 1, line 53, change "any" to --and--.

Column 5, line 10, change "spermacetic" to
--spermaceti--.

Column 6, line 63, change "93.70" to --98.70--.

Signed and sealed this 3rd day of October 1972.

(SEAL)

Attest:

EDWARD M. FLETCHER, JR.
Attesting Officer

ROBERT GOTTSCHALK
Commissioner of Patents