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(57) Abrégé/Abstract:
A cosmetic method is provided for reducing or inhibiting oil and grease generation from human skin by applying to the skin a C_{11}-C_{30} alkyl or alkenyl ester of salicylic acid as an active component in combination with a pharmaceutically acceptable carrier. Most preferred is tridecyl salicylate.

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(57) Abstract

A cosmetic method is provided for reducing or inhibiting oil and grease generation from human skin by applying to the skin a C_{11}–C_{30} alkyl or alkenyl ester of salicylic acid as an active component in combination with a pharmaceutically acceptable carrier. Most preferred is tridecyl salicylate.

METHOD FOR REDUCING SKIN OILS AND GREASE

BACKGROUND OF THE INVENTION

Field of the Invention

The invention relates to a method for controlling oil and grease secretion from skin.

The Related Art

Sebum is produced by the disruption of the cells in which it is formed (in the basal layer of the gland). This function may be termed holocrine secretion.

Being liquid inside the duct and hair follicle, sebum diffuses up and down the follicular canal. Upon reaching the skin surface it combines with epithelial lipids (from the keratinizing cells) and emulsifies as an oily liquid with water from the sweat glands. In this way a semi-solid, slightly acid, hydrophilic film is formed on the skin and in the hair follicles. The quantity of sebum produced is directly proportional to the size of the gland.

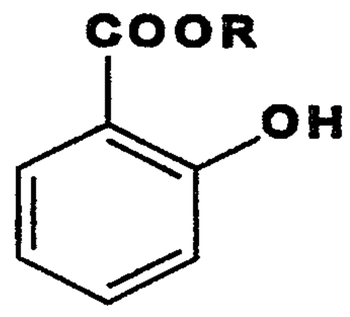
The rate of sebum production varies in different individuals, some having oilier skins than others. Male sex hormones increase sebum production. Increased temperature also increases production.

The literature is replete with methods and compositions for eliminating, treating or at least reducing the levels of skin oils and greasiness. None have proved totally satisfactory.

Accordingly, it is an object of the present invention to provide an improved method for controlling, reducing or inhibiting oiliness and greasiness in human skin. This and other objects of the present invention will become more fully apparent from the subsequent summary and detailed discussion.

SUMMARY OF THE INVENTION

A cosmetic method for reducing or inhibiting oiliness and greasiness in human skin is provided which involves topical application to the skin of a safe and effective amount of salicylate ester in a pharmaceutically acceptable carrier, the salicylate ester having the formula (I):



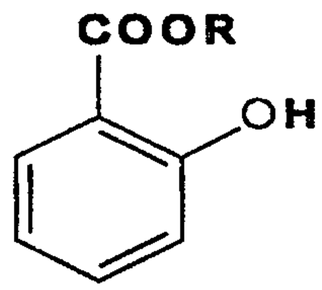
wherein R is a C_{11}-C_{30} alkyl or alkenyl radical.

The invention further provides the use of salicylate ester having the formula (I) above in reducing or inhibiting oiliness and greasiness in human skin.

The invention also comprises the use of a cosmetic composition comprising salicylate ester having formula I above, in a pharmaceutically acceptable carrier, in reducing or inhibiting oiliness and greasiness in human skin.

DETAILED DESCRIPTION OF THE INVENTION

Now it has been discovered that oil and grease production by skin may be controlled, reduced and/or inhibited through application of a cosmetic composition including as active a derivative of salicylic acid having formula (I):



wherein R is a C_{11}-C_{30} alkyl or alkenyl radical. Most preferred are the C_{12}-C_{20} alkyl or alkenyl, optimally the C_{13} alkyl or alkenyl esters of salicylic acid. By the term "skin" is meant to include all areas containing sebaceous glands, such as face, back, chest and scalp.

"Safe and effective amounts" of the C_{11}-C_{30} esters of salicylic acid are to be used within cosmetic compositions of the present invention. The term "safe and effective amounts" are defined as any amount sufficient to significantly induce a positive modification in lipid production but low enough to avoid any undesirable side effects (at a reasonable benefit/risk ratio), within the scope of sound medical judgement. The safe and effective amount of the salicylate esters will vary with the particular age and physical condition of the subject being evaluated, the severity of the condition, the duration of the treatment, the nature of concurrent therapy, the specific ester employed, the particular pharmaceutically-

acceptable carrier utilized, and like factors. Generally these amounts may range from 0.01 to 20%, preferably from 0.1 to 10%, more preferably from 1 to 8%, optimally from 2 to 6% by weight of the composition.

Besides the active salicylate ester, compositions of the present invention will utilize a pharmaceutically, physiologically and/or cosmetically acceptable carrier. The carrier may either be aqueous, anhydrous or an emulsion. Preferably the compositions are aqueous, especially water and oil emulsions of the W/O or O/W variety. Water when present will be in amounts which may range from 5 to 95%, preferably from 20 to 70%, optimally between 35 and 60% by weight.

Besides water, relatively volatile solvents may also serve as carriers within compositions of the present invention. Most preferred are monohydric C_1-C_3 alkanols. These include ethyl alcohol, methyl alcohol and isopropyl alcohol. The amount of monohydric alkanol may range from 1 to 70%, preferably from 10 to 50%, optimally between 15 to 40% by weight.

Emollient materials may also serve as pharmaceutically physiologically and/or cosmetically acceptable carriers. These may be in the form of silicone oils and synthetic esters. Amounts of the emollients may range anywhere from 0.1 to 50%, preferably between 1 and 20% by weight.

Silicone oils may be divided into the volatile and non-volatile variety. The term "volatile" as used herein refers to those materials which have a measurable vapor pressure at ambient temperature. Volatile silicone oils are preferably chosen from cyclic or linear polydimethyl-

siloxanes containing from 3 to 9, preferably from 4 to 5, silicon atoms.

Linear volatile silicone materials generally have viscosities less than 5 centistokes at 25°C while cyclic materials typically have viscosities of less than 10 centistokes.

Nonvolatile silicone oils useful as an emollient material include polyalkyl siloxanes, polyalkylaryl siloxanes and polyether siloxane copolymers. The essentially non-volatile polyalkyl siloxanes useful herein include, for example, polydimethyl siloxanes with viscosities of from 5 to 100,000 centistokes at 25°C. Among the preferred non-volatile emollients useful in the present compositions are the polydimethyl siloxanes having viscosities from 10 to 400 centistokes at 25°C.

Among the ester emollients are:

(1) Alkenyl or alkyl esters of fatty acids having 10 to 20 carbon atoms. Examples thereof include isoarachidyl neopentanoate, isononyl isonanonoate, oleyl myristate, oleyl stearate, and oleyl oleate.

(2) Ether-esters such as fatty acid esters of ethoxylated fatty alcohols.

(3) Polyhydric alcohol esters. Ethylene glycol mono and di-fatty acid esters, diethylene glycol mono- and di-fatty acid esters, polyethylene glycol (200-6000) mono- and di-fatty acid esters, propylene glycol mono- and di-fatty acid esters, polypropylene glycol 2000 monooleate, polypropylene glycol 2000 monostearate, ethoxylated propylene glycol monostearate, glyceryl mono- and di-fatty acid esters,

polyglycerol poly-fatty esters, ethoxylated glyceryl monostearate, 1,3-butylene glycol monostearate, 1,3-butylene glycol distearate, polyoxyethylene polyol fatty acid ester, sorbitan fatty acid esters, and polyoxyethylene sorbitan fatty acid esters are satisfactory polyhydric alcohol esters.

(4) Wax esters such as beeswax, spermaceti, myristyl myristate, stearyl stearate and arachidyl behenate.

(5) Sterols esters, of which cholesterol fatty acid esters are examples thereof.

Fatty acids having from 10 to 30 carbon atoms may also be included as pharmaceutically acceptable carriers for compositions of this invention. Illustrative of this category are pelargonic, lauric, myristic, palmitic, stearic, isostearic, hydroxystearic, oleic, linoleic, ricinoleic, arachidic, behenic and erucic acids.

Humectants of the polyhydric alcohol-type may also be employed as pharmaceutically acceptable carriers in compositions of this invention. The humectant aids in increasing the effectiveness of the emollient, reduces scaling, stimulates removal of built-up scale and improves skin feel. Typical polyhydric alcohols include glycerol, polyalkylene glycols and more preferably alkylene polyols and their derivatives, including propylene glycol, dipropylene glycol, polypropylene glycol, polyethylene glycol and derivatives thereof, sorbitol, hydroxypropyl sorbitol, hexylene glycol, 1,3-butylene glycol, 1,2,6-hexanetriol, ethoxylated glycerol, propoxylated glycerol and mixtures thereof. For best results the humectant is preferably propylene glycol. The amount of

humectant may range anywhere from 0.5 to 30%, preferably between 1 and 15% by weight of the composition.

Thickeners may also be utilized as part of the pharmaceutically acceptable carrier of compositions according to the present invention. Typical thickeners include crosslinked acrylates (e.g. Carbopol 982®), hydrophobically-modified acrylates (e.g. Carbopol 1382®), cellulosic derivatives and natural gums. Among useful cellulosic derivatives are sodium carboxymethylcellulose, hydroxypropyl methylcellulose, hydroxypropyl cellulose, hydroxyethyl cellulose, ethyl cellulose and hydroxymethyl cellulose. Natural gums suitable for the present invention include guar, xanthan, sclerotium, carrageenan, pectin and combinations of these gums. Amounts of the thickener may range from 0.0001 to 5%, usually from 0.001 to 1%, optimally from 0.01 to 0.5% by weight.

Collectively the water, solvents, silicones, esters, fatty acids, humectants and/or thickeners will constitute the pharmaceutically acceptable carrier in amounts from 1 to 99.9%, preferably from 80 to 99% by weight.

Cosmetic compositions of the present invention may be in any form. These forms may include emulsified systems such as lotions and creams, microemulsions, roll-on formulations, mousses, ointments (hydrophilic and hydrophobic), aerosol and non-aerosol sprays and pad-applied formulations.

Surfactants may also be present in cosmetic compositions of the present invention. Total concentration of the surfactant will range from 0.1 to 40%, preferably from 1 to 20%, optimally from 1 to 5% by weight of the composition. The surfactant may be selected from the group

consisting of anionic, nonionic, cationic and amphoteric actives. Particularly preferred nonionic surfactants are those with a C_{10}-C_{20} fatty alcohol or acid hydrophobe condensed with from 2 to 100 moles of ethylene oxide or propylene oxide per mole of hydrophobe; C_2-C_{10} alkyl phenols condensed with from 2 to 20 moles of alkylene oxide; mono- and di- fatty acid esters of ethylene glycol; fatty acid monoglyceride; sorbitan, mono- and di- C_8-C_{20} fatty acids; block copolymers (ethylene oxide/propylene oxide); and polyoxyethylene sorbitan as well as combinations thereof. Alkyl polyglycosides and saccharide fatty amides (e.g. methyl gluconamides) are also suitable nonionic surfactants.

Preferred anionic surfactants include soap, alkyl ether sulfate and sulfonates, alkyl sulfates and sulfonates, alkylbenzene sulfonates, alkyl and dialkyl sulfosuccinates, C_8-C_{20} acyl isethionates, acyl glutamates, C_8-C_{20} alkyl ether phosphates and combinations thereof.

Sunscreen actives may also be included in compositions of the present invention. Particularly preferred are such materials as ethylhexyl p-methoxycinnamate, available as Parsol MCX, and benzophenone-3, also known as Oxybenzone. Inorganic sunscreen actives may be employed such as microfine titanium dioxide, polyethylene and various other polymers. Amounts of the sunscreen agents will generally range from 0.1 to 30%, preferably from 2 to 20%, optimally from 4 to 10% by weight.

Preservatives can desirably be incorporated into the cosmetic compositions of this invention to protect against the growth of potentially harmful microorganisms. Suitable traditional preservatives for compositions of this invention are alkyl esters of para-hydroxybenzoic acid.

Other preservatives which have more recently come into use include hydantoin derivatives, propionate salts, and a variety of quaternary ammonium compounds. Cosmetic chemists are familiar with appropriate preservatives and routinely choose them to satisfy the preservative challenge test and to provide product stability. Particularly preferred preservatives are phenoxyethanol, methyl paraben, propyl paraben, imidazolidinyl urea, sodium dehydroacetate and benzyl alcohol. The preservatives should be selected having regard for the use of the composition and possible incompatibilities between the preservatives and other ingredients in the emulsion. Preservatives are preferably employed in amounts ranging from 0.01% to 2% by weight of the composition.

Compositions of the present invention may also contain water-soluble vitamins. The term water-soluble defines substances with a solubility of at least 0.1%, preferably at least 1%, optimally at least 5% by weight in water. Illustrative water-soluble vitamins are Niacin, Vitamin B_6, Vitamin C and Biotin. One source for Vitamin C is a product sold under the trademark of Vitazyme C available from the Brooks Company. Niacin, Vitamin B and Biotin are available from Roche Pharmaceuticals. Total amount of vitamins in compositions according to the present invention may range from 0.001 to 1%, preferably from 0.01 to 0.6, optimally from 0.1 to 0.5% by weight.

Keratolytic agents such as C_2-C_{25} α-hydroxy alkanoic acids may also be incorporated into compositions of this invention. Illustrative of this group of materials are glycolic, lactic, α-hydroxyoctanoic acids and salts thereof. The salts may be selected from alkalimetal, ammonium and C_1-C_{20} alkyl or alkanolammonium counterions.

Levels of α-hydroxyalkanoic acids may range from 0.001 to 10%, preferably between 0.2 and 1%, optimally between 0.4 and 0.5% by weight.

Minor adjunct ingredients may also be present in the cosmetic compositions. Among them may be the water-insoluble vitamins such as Vitamin A Palmitate, Vitamin E Acetate and DL-panthenol.

Another adjunct ingredient can be that of an enzyme. Particularly preferred is superoxide dismutase, commercially available as Biocell SOD from Brooks Industries, USA.

Natural vegetable materials from renewable resources are often desirable in cosmetic compositions. For instance, cosmetic compositions of the present invention may include β-glucan derived from oats, commercially available under the trademark Microat SF from Nurture Inc., Missoula, Montana.

Colorants, fragrances, opacifiers and abrasives may also be included in compositions of the present invention. Each of these substances may range from 0.05 to 5%, preferably between 0.1 and 3% by weight.

The following Examples will more fully illustrate embodiments of this invention.

All parts, percentages and proportions referred to herein and in the appended claims are by weight of the composition unless otherwise indicated.

EXAMPLE 1

The following skin oil and grease reducing sunscreen creme is prepared having a composition described in Table I.

TABLE I

COMPONENT	WEIGHT %
Carbopol 1382® (2% solids)	8.000
Spectron SA-13® (Tridecyl Salicylate)	6.000
Parsol MCX®	6.000
Isoarachidyl Neopentanoate	4.300
Benzophenone-3	3.000
Glycerin	3.000
Isononyl Isononanoate	2.500
Arlacel 165 VS® (GMS/PEG)	1.700
BRIJ 721® (Vegetable)	1.200
Isostearic Acid	1.200
Polymethyl Methacrylate	1.000
Cetyl Alcohol	1.000
Triethanolamine	0.770
Phenoxyethanol	0.700
Actiglyde-J Special® (Bio-hyaluronic acid)	0.500
Vitamin E Acetate	0.500
BRIJ 72® (Vegetable)	0.300
Methylparaben	0.300
Polyethylene (A-C 400)®	0.300
Algae Extract	0.250
Glydant®	0.200
DL-Panthenol	0.200
C_{12}-C_{20} Acid-PEG 8 Esters	0.200
Trilaureth-4-Phosphate	0.200
Silicone 200 (10cst)	0.200
Microat SF®	0.200
Niacin	0.200
Amigel®	0.170
Vitazyme C®	0.100
Superoxide Dismutase	0.100
Vitamin B_6	0.100
Vitamin A Palmitate	0.100
Propylparaben	0.100
Disodium EDTA	0.100
L-Lactic Acid	0.010
Biotin	0.001
Deionized Water	qs

EXAMPLE 2

Another skin oil and grease inhibiting creme is prepared having a composition described in Table II.

TABLE II

COMPONENT	WEIGHT %
Carbopol 1382® (2% Solids)	18.000
Cyclomethicone	6.000
Cetyl Alcohol	4.400
Spectron SA-13® (Tridecyl Salicylate)	4.000
Glycerin	3.000
Isoarachidyl Neopentanoate	2.400
Emulgade 1000 NI®	1.750
Willowbark Extract	1.500
Triethanolamine 99%	1.420
C_{18}-C_{36} Fatty Acid	1.200
BRIJ 721® (Vegetable)	1.200
Arachidyl Behenate	1.000
Actiglyde-J Special®	1.000
Polymethyl Methacrylate	1.000
Vitamin E Acetate	1.000
Sodium Pyrolidone Carboxylate (50% solids)	0.750
Algae Extract	0.500
DL-Panthenol	0.500
Silicone 200 (10 cst)	0.400
C_{12}-C_{20} Acid-PEG 8 Esters	0.400
Microat SF®	0.360
Bernel Ester TOC®	0.360
Glydant®	0.300
Methylparaben	0.300
BRIJ 72® (Vegetable)	0.300
Polyethylene (A-C 400)®	0.300
Shea Butter	0.200
Disodium EDTA	0.100
Amigel®	0.100
Propylparaben	0.100
Vitamin A Palmitate	0.100
L-Lactic Acid	0.010
Biotin	0.001
Vitazyme C®	0.001
Deionized Water	qs

EXAMPLE 3

The present Example reports an in vitro analysis of sebum suppression by use of a salicylate ester.

In Vitro Sebocyte Lipogenesis Assay

Human sebaceous glands were isolated from the nose of a male (age 60) and cultured using submerged tissue culture techniques (Bajor et al, J. Invest. Dermatol. 102:1994. P. 564). These sebocytes accumulate intracellular lipid droplets characteristic of mature human sebum.

Harvested and passaged sebocytes were added to each well of a 48 well tissue culture plate and incubated at 37°C in the presence of 7.5% CO_2 for 10 days. The growth medium was changed three times per week. On the day of experimentation, the growth medium was removed and the sebocytes washed three times with phosphate buffered saline (PBS). Fresh PBS in 0.5 ml amount was added to each well and 10 microliters of active agent speculated to inhibit lipogenesis. Triplicate wells were utilized for each sample. Controls consisted of PBS, dimethyl sulfoxide (DMSO) used to solubilize the lipophilic compounds, and phenol red, a compound which possesses estrogen-like activity. The cultures were incubated at 37°C/7.5% CO_2 for 30 minutes. Radioactive label was prepared by adding 100 µl of 14-C labelled acetic acid (Amersham, sodium salt, specific activity of 56 mCi/mmol) to 10 ml of 50 mM sodium acetate buffer. Then 50 µl was added to each well containing the sebocytes and active agents. The cultures were returned to the incubator for 4 hours. Thereafter the treatments and label were removed and the sebocytes rinsed

three times with fresh PBS. Sebocytes were harvested and 10 microliters removed and set aside for protein assessment. The remaining samples containing the 14-C label were extracted and the label counted using a Beckman scintillation counter. Triplicates were performed for each sample.

For each 48 well tissue culture plate, 16 samples could be analyzed. Of these, 1 sample was reserved for PBS, 1 sample for DMSO, and 1 sample for phenol red leaving 13 remaining samples.

TABLE I

Tridecylsalicylate Concentration	% Reduction	Standard Deviation
0.00003%	8.5	2.5
0.0003%	13.3	1.0
0.003%	28.3	2.1
0.01%	44.7	9.7
0.03%	49.1	6.3
0.05%	48.9	8.5
0.1%	63.0	7.7

TABLE II

Octylsalicylate Conc.	% Reduction	Standard Deviation
0.005%	11.6	12.2
0.01%	11.6	4.1
0.05%	22.4	15.1
0.1%	8.3	19.7
0.5%	0	12.6
1.0%	2.2	7.8
0.1% Phenol Red	40.8	12.5

TABLE III

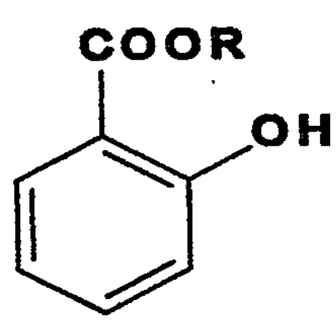
Salicylic Acid conc	% Reduction	Standard Deviation
0.00014%	11.4	9.0
0.0014%	10.1	10.5
0.014%	13.1	13.4
0.14%	3.6	7.4

Based on the results In Tables I, II and III, it is evident that tridecyl salicylate has significant activity in reducing oiliness and grease, especially compared to octylsalicylate and salicylic acid.

The foregoing description and examples illustrate selected embodiments of the present invention. In light thereof, various modifications will be suggested to one skilled in the art, all of which are within the spirit and purview of this invention.

WHAT IS CLAIMED IS:

1. A cosmetic method for reducing or inhibiting skin production of oils and grease, the method comprising applying to the skin a safe and effective amount of salicylate ester in a pharmaceutically physiologically and/or cosmetically acceptable carrier, the salicylate ester having the formula (I):



wherein R is a C_{11}-C_{30} alkyl or alkenyl radical.

2. The method according to claim 1 wherein the salicylate ester is a C_{12}-C_{20} alkyl ester of salicylic acid.

3. The method according to claim 1 wherein the salicylate ester is tridecyl salicylate.