



(51) International Patent Classification:

A61K 8/34 (2006.01) A61P 17/10 (2006.01)

A61K 31/05 (2006.01) A61P 17/08 (2006.01)

A61Q 19/00 (2006.01)

TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

- with international search report (Art. 21(3))
- in black and white; the international application as filed contained color or greyscale and is available for download from PATENTSCOPE

(21) International Application Number:

PCT/SG2020/050366

(22) International Filing Date:

25 June 2020 (25.06.2020)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

10201905850Q 25 June 2019 (25.06.2019) SG

(71) Applicant: AGENCY FOR SCIENCE, TECHNOLOGY AND RESEARCH [SG/SG]; 1 Fusionopolis Way, #20-10 Connexis North Tower, Singapore 138632 (SG).

(72) Inventors: LOW, Jun Xi, Selwyn; c/o Skin Research Institute of Singapore, 8A, Biomedical Grove, #05-33, Singapore 138648 (SG). LIM, Xinhong; c/o Skin Research Institute of Singapore, 8A, Biomedical Grove, #05-33, Singapore 138648 (SG). VAN STEENSEL, Maurice; c/o Skin Research Institute of Singapore, 8A, Biomedical Grove, #05-33, Singapore 138648 (SG). TAN, Kai Xuan, Keith; c/o Skin Research Institute of Singapore, 8A, Biomedical Grove, #05-33, Singapore 138648 (SG).

(74) Agent: VIERING, JENTSCHURA & PARTNER LLP; P.O. Box 1088, Rochor Post Office, Rochor Road, Singapore 911833 (SG).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM,

(54) Title: PHENOLS THAT DECREASE LIPID PRODUCTION IN SEBOCYTES

(57) Abstract: The present invention relates to phenol compounds for use in a method of decreasing lipid production in sebocytes; to compositions comprising at least such a compound; to the use of such a composition for decreasing lipid production in sebocytes; and to a cosmetic method for decreasing lipid production in sebocytes. In some embodiments, the compound is selected from the group consisting of bakuchiol and pterostilbene.



WO 2020/263189 A1

PHENOLS THAT DECREASE LIPID PRODUCTION IN SEBOCYTES

CROSS-REFERENCE TO RELATED APPLICATION

This application claims the benefit of priority of Singapore Patent Application No. 10201905850Q, filed 25 June 2019, the contents of which being hereby incorporated by reference in its entirety for all purposes.

FIELD OF THE INVENTION

The present invention relates to phenol compounds for use in a method of decreasing lipid production in sebocytes; to compositions comprising at least such a compound; to the use of such a composition for decreasing lipid production in sebocytes; and to a cosmetic method for decreasing lipid production in sebocytes.

BACKGROUND OF THE INVENTION

Consumers are increasingly interested in cosmetics that treat, mitigate, or delay the effects of excess lipids on their skin. The signs of excess lipids manifest themselves, for instance, in an unflattering oiliness and shine to the skin due to over-production of sebum. There is an active interest in the cosmetics industry to develop products that may be used to reduce the amount of lipids within the skin and thereby provide anti-oil/sebum benefits.

Sebum is an oily secretion of the sebaceous glands (sebocytes) of the skin that contains lipids (fat, triglycerides, and fatty acids), keratin, and cellular materials. Sebum normally constitutes a natural moisturizer for the epidermis maintaining its integrity. The level of sebum production varies from person to person and depends largely on sex and age. In particular, sebum production is influenced by hormones, i.e. androgens such as testosterone, and therefore occurs most prevalently in males during adolescence. During the teenage years, the complexion of the skin, i.e., the color and appearance of the skin, is oily primarily due to these hormonal changes. However, in both men and women sebum production can be stimulated by physical or emotional factors, which are altered by hormones. Besides age and sex factors, sebum production is also influenced by stress, use or consumption of pharmaceuticals and drugs such as muscle stimulants and/or the presence of disease states that interfere with the autonomic nervous system such as Parkinson's, strokes, etc.

Some people exhibit hyperseborrhoeic skin characterized by an exaggerated secretion and excretion of sebum. Generally, individuals with hyperseborrhoeic skin exhibit sebum levels of greater than 200

$\mu\text{g}/\text{cm}^2$ measured on the forehead. This overproduction of sebum may lead to aesthetic problems, such as oily/shiny skin or hair, acne-prone skin, enlarged pores, thickened skin, or poorer hold of makeup. Additionally, the excess sebum may act as a catalyst for acne by clogging pores leading to the formation of comedones ("blackheads" or "whiteheads"), which, when left untreated, may become inflamed and progress into acne vulgaris. Additionally, odors may be emitted as a result of excess sebum accumulation, production, or excretion.

The sebaceous glands are found over most of the body, although there are few on the hands or feet and none on the palms and soles. Sebaceous glands on the mid-back, forehead and chin are larger and more numerous than elsewhere (up to 400-900 glands per square centimetre). They are also numerous in the ear canal and around the genitals. The sebaceous gland consists of lobes connected by ducts, which are lined with cells similar to those on the skin surface. The sebum flow dynamics at the skin surface results from a multi-step process starting with sebocyte proliferation, intracellular lipid synthesis, cell lysis in the sebaceous duct, storage of sebum in the follicular reservoir, discharge through the follicular opening and spreading over the stratum corneum (Pierard, *Dermatology*, vol. 196, pages 126-129 (1998)). Most sebaceous glands open out into the hair follicle. Some free sebaceous glands open directly onto the skin surface. These include Meibomian glands on the eyelids, Tysons glands on the foreskin and Fordyces spots on the upper lip. Sebum is produced when the sebaceous gland disintegrates. The cells take about a week from formation to discharge.

The sebocyte constitutes the competent cell of the sebaceous gland. The production of sebum is associated with the program of terminal differentiation of this cell. During this differentiation, the metabolic activity of the sebocyte is essentially centered around the biosynthesis of lipids (lipogenesis), and more precisely on the neosynthesis of fatty acids and the squalene.

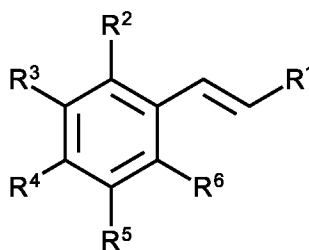
Generally, cosmetic treatments for excess lipid production provide relief from the symptoms, i.e., oiliness, enlarged pores, acne prone skin, irregular skin texture, etc., and fail to address the underlying cause. For example, the classic approach to addressing oily or shiny skin is the use of powders that provide an immediate masking effect by absorbing the excess sebum on the skin's surface. Additionally, various astringents and cleaning agents may be used to control sebum. However, all of these means for lipid reduction on the skin surface are limited, producing little sustainable visible results over extended periods of time. Astringents and cleaners may actually exacerbate the condition through a rebound effect. These means for combating excess and/or unwanted sebum are limited, and the need for additional approaches remains. Particularly, a compound capable of reducing the production of lipids constituting sebum, by the cells of the sebaceous gland (sebocytes), would be of definite value for the treatment of oily skin.

Consequently, in view of the above-discussed need, it is an object of the present invention to provide compounds, compositions, and methods for inhibiting excess lipid accumulation and/or over-production in sebocytes and/or the skin of an individual. It is a further object of the invention to

improve the overall appearance of skin affected by excess lipids or lipid over-production, including treatment, reversal, and/or prevention of oily skin and/or hair, acne-prone skin, body odors, enlarged pores, etc.

SUMMARY OF THE INVENTION

In a first aspect, the present invention thus relates to a compound according to Chemical Formula (I)



(I)

wherein, in Chemical Formula (I), R¹ is selected from the group consisting of C2-C15 (hetero)alkenyl, C2-C15 (hetero)alkynyl, C3-C15 (hetero)cycloalkyl, and (hetero)aryl,

and R², R³, R⁴, R⁵ and R⁶ are each independently selected from the group consisting of halogen, H, OH, SH, and C1-C10 (hetero)alkyl, preferably from the group consisting of halogen, H, OH, SH, OCH₃, OCF₃, CH₂OH, COOH, COOCH₃, and O(CO)CH₃;

or a pharmaceutically or cosmetically acceptable salt, prodrug, solvate, tautomer or stereoisomer thereof,

for use in a method of decreasing lipid production in sebocytes.

In a second aspect, the present invention relates to a composition comprising at least one compound, as defined herein, and at least one pharmaceutically or cosmetically acceptable carrier.

In a third aspect, the present invention relates to the use of a composition, as defined herein, for decreasing lipid production in sebocytes.

In a fourth aspect, the present invention relates to a cosmetic method for decreasing lipid production in sebocytes or in the skin of an individual in need thereof, comprising contacting said sebocyte or skin with a lipid production-decreasing amount of at least one compound, as defined herein, or composition, as defined herein.

BRIEF DESCRIPTION OF THE DRAWINGS

The invention will be better understood with reference to the detailed description when considered in conjunction with the non-limiting examples and the accompanying drawings.

Figure 1 depicts the plate reader data showing that bakuchiol and pterostilbene reduced lipid accumulation by about 20 % and 35 %, respectively. The fluorescent intensity for each compound treatment was compared against vehicle (DMSO) control treatment and EGCG (epigallocatechin gallate) as a comparative example compound.

Figure 2 depicts the flow cytometer data revealing that bakuchiol and pterostilbene reduced lipid accumulation by about 30 % and 15 %, respectively. DMSO (vehicle) was used as control and EGCG (epigallocatechin gallate) was used as a comparative example compound.

DETAILED DESCRIPTION

Embodiments of the present invention are described below, but the present invention is not limited thereto. It should be recognized that these embodiments are merely illustrative of the principles of the present invention. Numerous modifications and adaptations will be readily apparent to those of skill in the art without departing from the scope of the invention.

“At least one”, as used herein in relation to any component, refers to the number of chemically different molecules, i.e. to the number of different types of the referenced species, but not to the total number of molecules.

“One or more”, as used herein, relates to at least one and comprises 1, 2, 3, 4, 5, 6, 7, 8, 9 or more of the referenced species. Similarly, “at least one” means one or more, i.e. 1, 2, 3, 4, 5, 6, 7, 8, 9 or more.

In the present specification, the terms “a” and “an” and “at least one” are the same as the term “one or more” and can be employed interchangeably.

“About”, as used herein in relation to a numerical value, means said value $\pm 10\%$, preferably $\pm 5\%$.

All percentages given herein in relation to the compositions or formulations relate to weight % relative to the total weight of the respective composition or formula, if not explicitly stated otherwise.

As used herein, the term “an individual in need thereof” refers to an individual with a normal but noticeable and undesired skin condition, or unwanted feature, due to the excess presence or over-production of lipids, e.g. hyperseborrhoea, etc., or an individual that would like to decrease the presence or production of lipids in the absence of a noticeable and undesired skin condition, i.e. as a preventative or prophylactic such as for acne or clogged pores.

An “amount effective” or an “effective amount” to provide a particular benefit to the skin that may be correlated to a decrease in lipid production in sebocytes and that refers to the amount of phenol compound, as herein defined, required to provide a clinically measurable improvement in the particular manifestation of the lipid over-production, i.e., an unwanted feature associated with over-production of lipids, when applied or administered for a time sufficient to provide a clinically measurable improvement in the particular manifestation of lipid over-production. In other words, said terms are meant to refer to an amount required to elicit the biological or medical response of a cell, tissue, animal or human that is being sought, i.e. to effectuate a decrease in lipid production in the sebocyte and/or skin.

The terms “reducing lipid production” and “decreasing lipid production”, respectively, are used herein to mean a detectable lowering of the amount of lipids synthesized by a sebocyte exposed to a triterpenoid compound and/or composition comprising at least one such compound, as defined herein, as compared to the amount of lipids synthesized in the absence of such an inhibiting compound. The terms “reduction” and “decrease”, respectively, as used herein in relation to lipids are intended to refer to the complete prevention, control of secretion, or a degree of reduction (i.e. lowering) of the production of lipids, respectively. The term “lowering” may refer to about 10 % independently to about 100 % decrease in the amount of lipids synthesized. In some embodiments, the term “lowering” refers to about 15 % independently to about 95% decrease in the amount of lipids synthesized. In other embodiments, the term “lowering” refers to about 25 % independently to about 90 % decrease in the amount of lipids synthesized. In further embodiments, the term “lowering” refers to about 30% independently to about 85% decrease in the amount of lipids synthesized, and in still further embodiments, the term “lowering” refers to about 40% independently to about 80% decrease in the amount of lipids synthesized, or from 50% independently to about 75%, alternatively from 60% independently to about 70%. As used herein with respect to a range, “independently” means that any threshold may be used together with another threshold to give a suitable alternative range, e.g. 75% independently to about 90% is also considered a suitable alternative range.

The terms lowering, reducing, decreasing, suppressing and inhibiting, when used in relation to lipid production, are intended to be used interchangeably. Such reduction in lipid production may be evaluated subjectively or by using assays including, but not limited to, *in vitro*, *ex vivo*, animal models, and/or clinical models known to those skilled in the art. For example, the reduction of lipid production may be established using methods known to those skilled in the art including, but not limited to, human sebocyte cultures, Rat/mouse preputial models, hamster flank/ear models and or clinical models. See K. R. Smith and D. M. Thiboutot, *Thematic review series: Skin Lipids Sebaceous gland lipids: friend or foe?*, Journal of Lipid Research Volume 49, 2008 271. Further reference in this context is made to U.S. Patent Application Publication No. 20050053631.

“Prevention” as used herein, as well as related terms such as “prevent” or “preventing,” is meant to refer to provide skin not yet affected by the condition with a benefit that serves to avoid, delay,

forestall, minimize, or reduce the recurrence/onset of one or more unwanted features associated with the skin condition to be prevented. Such preventative benefits include, for example, delaying development and/or recurrence of the condition, or reducing the duration, severity, or intensity of one or more unwanted features associated with the condition if it eventually develops. Use of the term “prevention” is not meant to imply that all subjects in a subject population administered the compounds and/or (cosmetic) compositions described herein will never be affected by or develop the cosmetic or dermatologic conditions, damage, effect, or symptom, but rather that the subject population will exhibit a reduction in the cosmetic or dermatologic damages, effects, or symptoms. For example, many flu vaccines are not 100% effective at preventing flu in those administered the vaccine. Preventing lipid over-production refers to providing not yet affected skin with a benefit that serves to avoid, delay, forestall, or minimize one or more unwanted features associated with lipid over-production, such as reducing the extent of oiliness or severity of acne, that would otherwise develop at the treated area in the absence of treatment.

The term “reducing the appearance of excess lipids” is meant herein to refer to any detectable reduction in skin lipids, e.g., a reduction visible to the naked eye, that occurs after contacting the skin of an individual with a phenol compound or treatment regimen comprising such a compound. As a non-limiting example, this may refer to the oiliness/shine of hyperseborrheic skin.

The term “skin” as used herein includes the skin on or in the face, mouth, neck, chest, back, arms, hands, legs, and scalp.

“Treatment” as used herein, as well as related terms such as “treat” or “treating,” refers to eradicating, reducing, ameliorating, or reversing one or more of the unwanted features associated with the skin condition being treated, such that the consumer perceives an improvement in the appearance of the skin or other treatment benefit with respect to the condition. Treating lipid over-production refers to eradicating, reducing, ameliorating, or reversing one or more of the unwanted features associated with over-production of lipids. Unwanted features associated with over-production of sebum, e.g., include oily, shiny, acne-prone skin, oily scalp, oily hair, dandruff-prone hair, enlarged pores, or undesirable body odors associated with the over-production of lipids. Treatment benefits include, without limitation, e.g., reducing the oily appearance of affected skin or hair, controlling surface oil, balancing sebum in oily-prone skin, visibly minimizing pores, reducing the incidence of acne (i.e., clogged pores, comedones, acne vulgaris, acne lesions, cystic acne, etc.), and even reducing undesirable body odor due to accumulation of excess sebum.

By “cosmetically acceptable” and “pharmaceutically acceptable”, respectively, it is meant that a particular compound or component is generally regarded as safe and nontoxic at the levels employed for cosmetic and/or pharmaceutical use.

The term "pharmaceutically or cosmetically acceptable salt", as used herein, is meant to include salts of active compounds, which are prepared with relatively nontoxic acids or bases, depending on the particular substituent moieties found on the compounds described herein. When compounds of the disclosure contain relatively acidic functionalities, base addition salts can be obtained by contacting the neutral form of such compounds with a sufficient amount of the desired base, either neat or in a suitable inert solvent. Examples of pharmaceutically acceptable base addition salts include sodium, potassium, calcium, ammonium, organic amino, or magnesium salt, or a similar salt. For more specific, non-limiting examples see, for instance, Berge *et al.*, "Pharmaceutical Salts", Journal of Pharmaceutical Science, 1977, 66, 1-19).

The neutral forms of the compounds may be regenerated by contacting the salt with a base or acid, respectively, and isolating the parent compound in the conventional manner. The parent form of the compound differs from the various salt forms in certain physical properties, such as solubility in polar solvents.

Certain compounds of the disclosure can exist in unsolvated forms as well as solvated forms ("solvates"), including hydrated forms. In general, the solvated forms are equivalent to unsolvated forms and are encompassed within the scope of the disclosure. Certain compounds of the disclosure may exist in multiple crystalline or amorphous forms. In general, all physical forms are equivalent for the uses contemplated by and are intended to be within the scope of the disclosure.

Certain compounds of the disclosure possess asymmetric carbon atoms (optical or chiral centers) or double bonds; the enantiomers, racemates, diastereomers, tautomers, geometric isomers, stereoisomeric forms that may be defined, in terms of absolute stereochemistry, as (R)- or (S)- or, as (D)- or (L)- for amino acids, and individual isomers are encompassed within the scope of the disclosure. The compounds of the disclosure do not include those, which are known in the art to be too unstable to synthesize and/or isolate. The disclosure is meant to include compounds in racemic and optically pure forms. Optically active (R)- and (S)- isomers may be prepared using chiral synthons or chiral reagents, or resolved using conventional techniques. When the compounds described herein contain olefinic bonds or other centers of geometric asymmetry, and unless specified otherwise, it is intended that the compounds include both E and Z geometric isomers.

The term "tautomer," as used herein, refers to one of two or more structural isomers which exist in equilibrium and which are readily converted from one isomeric form to another. It will be apparent to one skilled in the art that certain compounds of the disclosure may exist in tautomeric forms, all such tautomeric forms of the compounds being within the scope of the disclosure.

Unless otherwise stated, structures depicted herein are also meant to include all stereochemical forms of the structure; i.e., the R and S configurations for each asymmetric center. Therefore, single

stereochemical isomers as well as enantiomeric and diastereomeric mixtures of the present compounds are within the scope of the disclosure.

Unless otherwise stated, structures depicted herein are also meant to include compounds, which differ only in the presence of one or more isotopically enriched atoms. For example, compounds having the present structures except for the replacement of a hydrogen by a deuterium or tritium, or the replacement of a carbon by ^{13}C - or ^{14}C -enriched carbon are within the scope of the disclosure.

The term “prodrug”, as used herein, refers to a compound, which is in a prodrug form. Prodrugs of the compounds described herein are those compounds that readily undergo chemical changes under physiological conditions to provide the compounds of the disclosure.

Prodrug forms of the herein disclosed compounds are designed to improve their physicochemical properties (e.g. solubility, hydrophilicity, stability) and pharmacokinetic behavior (e.g. absorption, distribution, metabolism, excretion and toxicity). Prodrugs of the herein disclosed compounds can be designed for enrichment in the target cells, tissues or organs (e.g. skin).

Prodrug design strategies can be carrier-linked (i.e., they carry promoieties), can comprise spacers or can represent conjugates with biomacromolecules. Prodrug forms of the herein disclosed compounds can be mono-, double-, triple- (or multiple) prodrugs as well as mono-, bi-, tri- (or multi-) functional prodrugs. They can be bioactivated by physicochemical or enzymatic mechanisms.

Additionally, prodrugs can be converted to the compounds of the disclosure by chemical or biochemical methods in an *ex vivo* environment. For example, prodrugs can be slowly converted to the compounds of the disclosure when placed in a transdermal patch reservoir with a suitable enzyme or chemical reagent.

In the context of prodrugs, reference is generally made to marketed prodrugs such as Fosphenytoin, Pivampicillin and Bacampicillin. For more prodrug examples, see J. Med. Chem. 2004, 47(10):2393-404 and Nat. Rev. Drug Discov. 2018, 17(8):559-587.

The term “alkyl”, by itself or as part of another substituent, means, unless otherwise stated, a straight (i.e. linear, unbranched) or branched chain, or combination thereof, which is fully saturated and can include di- and multivalent radicals, having the number of carbon atoms designated (i.e. C1-C15 means one to fifteen carbons). Examples of saturated hydrocarbon radicals include, but are not limited to, groups such as methyl, ethyl, n-propyl, isopropyl, n-butyl, t-butyl, isobutyl, sec-butyl, cyclohexyl, (cyclohexyl)methyl, cyclopropylmethyl, homologs and isomers of, for example, n-pentyl, n-hexyl, n-heptyl, n-octyl, and the like.

The term “heteroalkyl,” by itself or in combination with another term, means, unless otherwise stated, a stable linear or branched hydrocarbon chain consisting of at least one carbon atom and at least one heteroatom selected from the group consisting of O, N, P, Si and S, and wherein the nitrogen and sulfur atoms may optionally be oxidized and the nitrogen heteroatom may optionally be quaternized. The heteroatom(s) O, N, P and S and Si may be placed at any interior position of the heteroalkyl group or at the position at which the alkyl group is attached to the remainder of the molecule. Examples include, but are not limited to, $\text{—CH}_2\text{—CH}_2\text{—O—CH}_3$, $\text{—CH}_2\text{—CH}_2\text{—NH—CH}_3$, $\text{—CH}_2\text{—CH}_2\text{—N(CH}_3\text{)—CH}_3$, $\text{—CH}_2\text{—S—CH}_2\text{—CH}_3$, $\text{—CH}_2\text{—CH}_2\text{—S(O)—CH}_3$, $\text{—CH}_2\text{—CH}_2\text{—S(O)}_2\text{—CH}_3$, —CH=CH—O—CH_3 , $\text{—Si(CH}_3\text{)}_3$, $\text{—CH}_2\text{—CH=N—OCH}_3$, $\text{—CH=CH—N(CH}_3\text{)—CH}_3$, O—CH_3 , $\text{—O—CH}_2\text{—CH}_3$, and —CN . Up to two heteroatoms may be consecutive, such as, for example, $\text{—CH}_2\text{—NH—OCH}_3$ and $\text{—CH}_2\text{—O—Si(CH}_3\text{)}_3$. As described above, heteroalkyl groups, as used herein, include those groups that are attached to the remainder of the molecule through a heteroatom, such as —C(O)R' , —C(O)NR' , —NR'R'' , —OR' , —SR' , and/or $\text{—SO}_2\text{R'}$. Where “heteroalkyl” is recited, followed by recitations of specific heteroalkyl groups, such as —NR'R'' or the like, it will be understood that the terms heteroalkyl and —NR'R'' are not redundant or mutually exclusive. Rather, the specific heteroalkyl groups are recited to add clarity. Thus, the term “heteroalkyl” should not be interpreted herein as excluding specific heteroalkyl groups, such as —NR'R'' or the like.

The terms “cycloalkyl” and “heterocycloalkyl”, by themselves or in combination with other terms, represent, unless otherwise stated, cyclic versions of “alkyl” and “heteroalkyl”, respectively. Additionally, for heterocycloalkyl, a heteroatom can occupy the position at which the heterocycle is attached to the remainder of the molecule. Examples of cycloalkyl include, but are not limited to, cyclopentyl, cyclohexyl, 1-cyclohexenyl, 3-cyclohexenyl, and the like. Examples of heterocycloalkyl include, but are not limited to, 1-(1,2,5,6-tetrahydropyridyl), 1-piperidinyl, 2-piperidinyl, 3-piperidinyl, 4-morpholinyl, 3-morpholinyl, tetrahydrofuran-2-yl, tetrahydrofuran-3-yl, tetrahydrothien-2-yl, tetrahydrothien-3-yl, 1-piperazinyl, 2-piperazinyl, and the like.

The terms “halo” or “halogen,” by themselves or as part of another substituent, mean, unless otherwise stated, a fluorine, chlorine, bromine, or iodine atom. According to some preferred embodiments, the halogen is fluorine.

The term “aryl” means, unless otherwise stated, a polyunsaturated, aromatic, hydrocarbon substituent which can be a single ring or multiple rings (such as 1 to 3 rings), which are fused together or linked covalently. The term “heteroaryl” refers to aryl groups (or rings) that contain from one to four heteroatoms selected from N, O, and S, preferably selected from O and S, wherein the nitrogen and sulfur atoms are optionally oxidized, and the nitrogen atom(s) are optionally quaternized. A heteroaryl group can be attached to the remainder of the molecule through a carbon or heteroatom. Non-limiting examples of aryl and heteroaryl groups include phenyl, 1-naphthyl, 2-naphthyl, 4-biphenyl, 1-pyrrolyl, 2-pyrrolyl, 3-pyrrolyl, 3-pyrazolyl, 2-imidazolyl, 4-imidazolyl, pyrazinyl, 2-oxazolyl, 4-oxazolyl, 2-phenyl-4-oxazolyl, 5-oxazolyl, 3-isoxazolyl, 4-isoxazolyl, 5-isoxazolyl, 2-thiazolyl, 4-thiazolyl, 5-

thiazolyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, 2-pyrimidyl, 4-pyrimidyl, 5-benzothiazolyl, purinyl, 2-benzimidazolyl, 5-indolyl, 1-isoquinolyl, 5-isoquinolyl, 2-quinoxaliny, 5-quinoxaliny, 3-quinolyl, and 6-quinolyl. Substituents for each of the above noted aryl and heteroaryl ring systems are selected from the group of acceptable substituents described below. According to various embodiments, the term “aryl” refers to a polyunsaturated, aromatic, hydrocarbon substituent containing up to 10 carbon atoms.

Where a heteroalkyl, heterocycloalkyl, or heteroaryl, for instance, includes a specific number of members (e.g. “3 to 7 membered”), the term “member” refers to a carbon or heteroatom.

The term “oxo” as used herein means an oxygen that is double bonded to a carbon atom.

Each of the above terms (e.g., “alkyl”, “heteroalkyl”) are meant to include both substituted and unsubstituted forms of the indicated radical, unless stated otherwise. Preferred substituents for each type of radical are provided below.

Substituents for the alkyl, heteroalkyl, alkenyl, heteroalkenyl, alkynyl, heteroalkynyl, cycloalkyl, heterocycloalkyl, cycloalkenyl, and heterocycloalkenyl radicals can be one or more of a variety of groups selected from, but not limited to: $\text{—OR}'$, $\text{—R}'\text{—O—R}''$, =O , $\text{—SR}'$, -halogen, $\text{—SiR}'\text{R}''\text{R}'''$, $\text{—OC(O)R}'$, $\text{—C(O)R}'$, $\text{—CO}_2\text{R}'$, $\text{—S(O)R}'$, $\text{—S(O)}_2\text{R}'$, unsubstituted C1-C6 (hetero)alkyl, and unsubstituted C2-C6 (hetero)alkenyl, in a number ranging from zero to $(2m'+1)$, where m' is the total number of carbon atoms in such a radical; wherein, in each of the aforementioned hydrocarbon groups, including R' , R'' , and R''' , one or more hydrogen atoms may be replaced by a halogen, preferably fluorine atom. R' , R'' , and R''' each independently refer to hydrogen, unsubstituted C1-C4 (hetero)alkyl, or unsubstituted C2-C4 (hetero)alkenyl. When a compound of the invention includes more than one R group, for example, each of the R groups is independently selected as are each R' , R'' , and R''' groups when more than one of these groups is present. From the above discussion of substituents, one of skill in the art will understand that the term “alkyl” is meant to include groups including carbon atoms bound to groups other than hydrogen groups, such as haloalkyl (e.g., —CF_3 and $\text{—CH}_2\text{CF}_3$) and acyl (e.g., —C(O)CH_3 , —C(O)CF_3 , $\text{—C(O)CH}_2\text{OCH}_3$, and the like). Illustrative examples of the aforementioned substituents include, but are not limited to: halogen, preferably F, OCF_3 , OC(O)CF_3 , C(O)OCF_3 (i.e. CO_2CF_3), CF_3 , OH, SH, OCH_3 , CH_3 , CH_2CH_3 , OC(O)CH_3 , C(O)OH , C(O)OCH_3 , CH_2OH , and $\text{C(CH}_3)_2\text{OH}$.

Similar to the substituents described for the alkyl radical, substituents for the aryl and heteroaryl groups are varied and are selected from, for example: halogen, $\text{—OR}'$, $\text{—SR}'$, -halogen, $\text{—SiR}'\text{R}''\text{R}'''$, $\text{—OC(O)R}'$, $\text{—C(O)R}'$, $\text{—CO}_2\text{R}'$, $\text{—S(O)R}'$, $\text{—S(O)}_2\text{R}'$, $\text{—R}'$, unsubstituted C1-C6 (hetero)alkyl, unsubstituted C2-C6 (hetero)alkenyl, in a number ranging from zero to the total number of open valences on the aromatic ring system; wherein, in each of the aforementioned hydrocarbon groups, including R' , R'' , and R''' , one or more hydrogen atoms may be replaced by a halogen, preferably

fluorine atom; and wherein R', R'', and R''' each independently refer to hydrogen, unsubstituted C1-C4 (hetero)alkyl, unsubstituted C2-C4 (hetero)alkenyl, unsubstituted C3-C6 (hetero)cycloalkyl, or unsubstituted C6-C10 aryl. When a compound of the invention includes more than one R group, for example, each of the R groups is independently selected as are each R', R'', and R''' groups when more than one of these groups is present.

As used herein, the term "heteroatom" or "ring heteroatom" is meant to include oxygen (O), nitrogen (N), sulfur (S), phosphorus (P), and silicon (Si).

The term "alkenyl" as used herein is a hydrocarbon group with a structural formula containing at least one carbon-carbon double bond. Asymmetric structures such as (A1A2)C=C(A3A4) are intended to include both the E and Z isomers. The alkenyl group can be substituted with one or more substituent groups, as described herein above. Unless stated otherwise, an alkenyl group, in the context of the present invention, may be branched or unbranched.

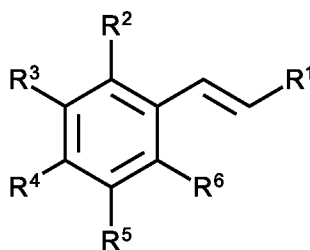
The term "cycloalkenyl" as used herein is a non-aromatic carbon-based ring composed of at least three carbon atoms and containing at least one carbon-carbon double bond, i.e., C=C. Examples of cycloalkenyl groups include, but are not limited to, cyclopropenyl, cyclobutenyl, cyclopentenyl, cyclopentadienyl, cyclohexenyl, and the like. The cycloalkenyl group can be substituted or unsubstituted, unless stated otherwise. The cycloalkenyl group can be substituted, unless stated otherwise, with one or more groups as described herein above.

The term "alkynyl" as used herein is a hydrocarbon group with a structural formula containing at least one carbon-carbon triple bond. The alkynyl group can be unsubstituted or substituted with one or more groups as described herein above. Unless stated otherwise, an alkynyl group, in the context of the present invention, may be branched or unbranched.

The term "hydrophilic group" as used herein is meant to refer, in the context of the present invention, to a group, which significantly interacts with water and exhibits a significant affinity for water. Non-limiting examples of hydrophilic groups include a hydroxyl group (-OH), a carboxy group (-COOH), a mercapto group (-SH), a sulfonic acid group (-SO₂OH), a hydroxyl- and/or carboxy-substituted alkyl group, such as CH₂OH or CH₂C(O)OCH₃, and the like.

The present inventors surprisingly found that certain phenol compounds allow for a reduction in lipids produced by sebocytes. Particularly, it was discovered that phenol compounds represented by Chemical Formula (I), as defined herein below, efficiently reduce lipid production in sebocytes.

Accordingly, in a first aspect, the present invention relates to a compound according to Chemical Formula (I)



(I)

wherein, in Chemical Formula (I), R¹ is selected from the group consisting of C2-C15 (hetero)alkenyl, C2-C15 (hetero)alkynyl, C3-C15 (hetero)cycloalkyl, and (hetero)aryl, and R², R³, R⁴, R⁵ and R⁶ are each independently selected from the group consisting of halogen, H, OH, SH, and C1-C10 (hetero)alkyl, preferably from the group consisting of halogen, H, OH, SH, OCH₃, OCF₃, CH₂OH, COOH, COOCH₃, and O(CO)CH₃; or a pharmaceutically or cosmetically acceptable salt, prodrug, solvate, tautomer or stereoisomer thereof, for use in a method of decreasing lipid production in sebocytes.

Without wishing to be bound by theory, it is believed that the phenol compounds disclosed herein may inhibit enzymes involved in the production of sebum lipids such as fatty acid, squalene and wax esters. It is further known that retinoids, which are structurally similar to the phenol compounds of the present invention, can counteract Wingless signaling by affecting gene transcription, possibly affecting sebum production by affecting sebaceous gland differentiation.

According to various embodiments, substituents, if present, of the above-indicated substituent groups R¹, R², R³, R⁴, R⁵, and R⁶ are preferably selected from the group consisting of OH, SH, OCH₃, COOH, COOCH₃, and O(CO)CH₃.

According to preferred embodiments, in the above Chemical Formula (I), at least one of R¹, R², R³, R⁴, R⁵, and R⁶, preferably at least two of R¹, R², R³, R⁴, R⁵, R⁶, R⁷, and R⁸, more preferably at least one of R¹, R³, and R⁵, more preferably at least two of R¹, R³, and R⁵ denote a hydrophilic substituent group, as herein defined. According to some embodiments, at least three of R¹, R², R³, R⁴, R⁵, and R⁶, more preferably at least three of R¹, R³, and R⁵ denote a hydrophilic group, as herein defined. Particularly, a respective hydrophilic substituent group may be selected from the group consisting of OH, SH, OCH₃, OCF₃, COOH, and PhOH, where applicable, more preferably from the group consisting of OH, OCH₃, OCF₃, and PhOH, respectively.

Without wishing to be bound by theory, it is believed that at least one, preferably at least two, more preferably at least three hydrophilic substituent groups positioned at the above-indicated positions of Chemical Formula (I) play a key role in reducing lipid production in sebocytes.

According to various embodiments, in Chemical Formula (I), R^1 is selected from the group consisting of C2-C15 alkenyl, and aryl; and R^2 , R^3 , R^4 , R^5 and R^6 are each independently selected from the group consisting of halogen, H, OH, SH, OCH_3 , OCF_3 , CH_2OH , $COOH$, $COOCH_3$, and $O(CO)CH_3$, preferably from the group consisting of H, OH, OCH_3 , CH_2OH , $COOH$, $COOCH_3$, and $O(CO)CH_3$. According to some embodiments, substituents, if present, if the aforementioned group R^1 may be selected from the group consisting of OH, OCH_3 , $COOH$, $COOCH_3$, and $O(CO)CH_3$.

In some embodiments, R^2 , R^3 , R^4 , R^5 and R^6 are not all H.

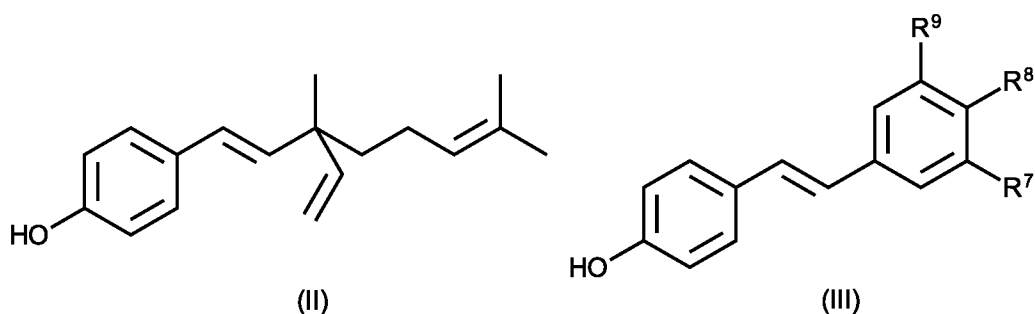
According to further embodiments, R^4 is OH or SH, preferably OH.

In various embodiments, R^4 is OH or SH, preferably SH; and R^2 , R^3 , R^5 and R^6 are each independently H or F, preferably H.

According to various further embodiments, R^1 is selected from the group consisting of C2-C10 alkenyl, and substituted phenyl, with substituents of the aforementioned groups being independently selected from the group consisting of halogen, OH, SH, OCH_3 , OCF_3 , $COOH$, $COOCH_3$, and $COOCF_3$, preferably from the group consisting of OH, SH, OCH_3 , OCF_3 , $COOH$, $COOCH_3$, and $COOCF_3$, more preferably from the group consisting of OH, OCH_3 , $COOH$, and $COOCH_3$.

In some embodiments, R^1 is selected from the group consisting of substituted or unsubstituted, branched C4-C10 alkenyl, and substituted phenyl, with substituents of the aforementioned groups being independently selected from the group consisting of OH, SH, OCH_3 , and OCF_3 , preferably from the group consisting of OH and OCH_3 .

In some embodiments, the compound is a compound corresponding to Chemical Formula (II) or Chemical Formula (III)



wherein, in Chemical Formula (III), R^7 , R^8 and R^9 are each independently selected from the group consisting of H, F, OH, SH, OCH_3 , and OCF_3 , preferably from the group consisting of H, OH, and OCH_3 .

In other embodiments, the compound is selected from the group consisting of bakuchiol and pterostilbene.

The herein disclosed and described compounds are intended for use in a method decreasing lipid production in sebocytes. According to various embodiments, overproduction (i.e. excess production) of lipids in sebocytes may be correlated to a skin disease or disorder. Thus, according to various embodiments, the herein described and disclosed compounds are for use in a method of treating a skin disease or disorder, and according to some embodiments, the method is the treatment of a skin disease or disorder related to increased lipid production in sebocytes. According to various embodiments, particularly, said skin disease or disorder is selected from the group consisting of oily skin, shiny skin, skin having whiteheads and/or blackheads, skin having enlarged pores, and acne.

The amount of compound according to the present invention, i.e. according to Chemical Formula (I), for use according to the present invention, i.e. as herein disclosed, generally depends on the desired effect, and can therefore vary within a large range, this amount being within the skill of the ordinary artisan in view of this disclosure. To give an order of magnitude, the compound can be used, for instance, in an amount in the range of about 0.0001 to 50.0 wt.-%, based on the total weight of a composition, preferably in an amount in the range of about 0.01 to 30.0 wt.-%, for instance in an amount in the range of about 0.1 to 25.0 wt.-%, based on the total weight of a composition.

As has been further discovered by the present inventors, a compound as herein defined as described, i.e. a compound according to Chemical Formula (I) of the present invention, may further be used, i.e. contacted with sebocytes and/or the skin of an individual, in the form of a plant extract comprising at least one such compound, as herein defined. Thus, according to various embodiments, whenever reference is made to a compound, as herein defined and described, i.e. a compound according to Chemical Formula (I), reference is also made to a plant extract comprising at least one such compound. For instance, but without limitation, as will be herein described below in more detail, a compound according to Chemical Formula (I) of the present invention may be comprised in a composition according to the present invention, and, accordingly, in the context of the present invention, a composition comprising at least one plant extract comprising at least one compound according to Chemical Formula (I), as herein described and defined, is also envisaged and thus falling within the scope of the invention.

According to various embodiments, a plant extract comprising at least one compound according to Chemical Formula (I), as herein defined and described, contains this at least one compound in an amount ranging from about 0.00001 wt.-% to about 99.9 wt.-%, preferably in an amount ranging from about 0.0001 wt.-% to about 95 wt.-%, more preferably in an amount of about 0.001 wt.-% to about 95 wt.-%, particularly in an amount of about 0.01 wt.-% to about 95 wt.-%, most preferably in an amount of at least 0.1 wt.-%, such as about 0.2, 0.5, 1.0, 1.5, 2.0, 2.5, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35,

40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90 or about 95 wt.-%, based on the total weight of the plant extract.

According to various embodiments, a plant extract comprising at least one compound according to Chemical Formula (I), as herein defined and described above, may be selected from the group consisting of extracts of plants belonging to the genus *Phtholobium*, *Psoralea* and *Pterocarpus*. According to various embodiments, a plant extract comprising at least one compound according to Chemical Formula (I) of the present invention may be selected from the group consisting of *Phtholobium pubescens*, *Psoralea corylifolia* seed, *Psoralea grandulosa* leaves, *Psoralea drupaceae*, *Ulmus davidiana* (bark of root and stem), *Phtholobium pubescens*, *Piper longum*, *Aerva sanguinolenta* Blume *Pterocarpus marsupium* (heartwood) and *Vaccinium species* (berries), grape leaves and vines and almonds.

For topical application to the skin, the sebum reducing agents of the present invention, i.e. the compounds according to Chemical Formula (I) defined above, may be provided in any cosmetic or pharmaceutical form normally used in the cosmetics and dermatological fields.

Thus, in another aspect, the present invention further relates to a composition comprising at least one compound according to Chemical Formula (I), as defined and described herein above, and at least one pharmaceutically or cosmetically acceptable carrier.

According to various embodiments, a composition according to the present invention is a topical composition, a cosmetic composition and/or a dermatological composition.

It may, in particular, be in the form of an aqueous, optionally gelled, solution, of a dispersion of the optionally two-phase lotion type, of an emulsion obtained by dispersion of a fatty phase (oil) in an aqueous phase (O/W) or *vice versa* (W/O), of a triple emulsion (W/O/W or O/W/O) or of a vesicular dispersion of the ionic and/or nonionic type. These compositions may be prepared according to the usual methods. Compositions according to the present invention may be more or less fluid and have the form of an emulsion, a cream, an ointment, a milk, a lotion, a serum, a paste, or a mousse. A composition according to the present invention may optionally be applied in the form of an aerosol. It may also be provided in solid form, in particular in the form of a stick. It may be used as a care product and/or as a cosmetic product for the skin. It may also be used as a shampoo or a conditioner.

The compounds of Chemical Formula (I), as herein described and defined, can be formulated in various cosmetic and pharmaceutical consumer products utilizing a variety of delivery systems and carrier bases, depending on the desired form of end-use. As more particular examples of consumer product forms anticipated by the present disclosure, shampoos, aftershaves, sunscreens, body and hand lotions, skin creams, liquid soaps, bar soaps, bath oil bars, shaving creams, conditioners, permanent waves, hair relaxers, hair bleaches, hair detangling lotion, styling gel, styling glazes, spray

foams, styling creams, styling waxes, styling lotions, mousses, spray gels, pomades, shower gels, bubble baths, hair coloring preparations, conditioners, hair lighteners, coloring and non-coloring hair rinses, hair grooming aids, hair tonics, spritzes, styling waxes, band-aids, and balms may be mentioned.

In various embodiments, the at least one compound according to Chemical Formula (I), as herein defined above, is present in an amount of at least about 0.05 wt.-%, preferably in an amount of at least about 0.1 wt.-%, based on the total weight of the composition. For instance, but without limitation, the at least one compound according to Chemical Formula (I), as herein defined above, is present in an amount of at least about 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1.0, 1.5, 2.0, 2.5, 3.0, 3.5, 4.0, 4.5, 5.0, 5.5, 6.0, 6.5, 7.0, 7.5, 8.0, 8.5, 9.0, 9.5, 10.0, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 wt.-%, and any ranges thereinbetween, based on the total weight of the composition.

According to some embodiments, the at least one compound according to Chemical Formula (I), as herein defined above, is present in a composition according to the present invention an amount of about 0.05 independently to 50 wt.-%, preferably in an amount of about 0.1 independently to 40 wt.-%, more preferably in an amount of about 0.1 independently to 30 wt.-%, even more preferably in an amount of about 0.5 independently to 25 wt.-%, based on the total weight of the composition.

Further, according to various embodiments, a plant extract containing one or more compounds, as disclosed and defined herein above, can be present in a composition according to the present invention, for instance and without limitation, in an amount in the range of about 0.0001 independently to 20 wt.-%, and any ranges thereinbetween based on the total weight of said composition.

For instance, but without limitation, the at least one plant extract containing at least one compound according to Chemical Formula (I), as herein defined above, is present in an amount of at least about 0.0001, 0.001, 0.01, 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1.0, 1.5, 2.0, 2.5, 3.0, 3.5, 4.0, 4.5, 5.0, 5.5, 6.0, 6.5, 7.0, 7.5, 8.0, 8.5, 9.0, 9.5, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 wt.-%, and any ranges thereinbetween based on the total weight of the composition.

In some embodiments, the herein described delivery system may be in the form of a traditional water and oil emulsion, a suspension, a colloid, a micro emulsion, a clear solution, a suspension of nanoparticles, an emulsion of nanoparticles, or an anhydrous composition.

The compositions that contain the compound of the present invention may also contain adjuvants, which are used in the cosmetics field, such as hydrophilic or lipophilic gelling agents, hydrophilic or lipophilic active agents, preserving agents, antioxidants, solvents, fragrances, fillers, screening agents, pigments, odor absorbers and dyestuffs. The amounts of these various adjuvants may be those conventionally used in the field considered. These adjuvants, depending on their nature, can be

introduced into the fatty phase, into the aqueous phase or into the lipid vesicles. In addition, moisturizers may complete the effect obtained using the compounds according to the present invention. A further class of useful ingredients are anti-inflammatory agents.

Preferably, however, a composition according to the present invention further, i.e. in addition to the at least one compound according to Chemical Formula (I), comprises one or more excipient, i.e. one or more pharmaceutically or cosmetically acceptable carrier, which may be selected from, but is not limited to, the group consisting of water, saccharides, surface active agents, humectants, petrolatum, mineral oil, fatty alcohols, fatty ester emollients, waxes and silicone-containing waxes, silicone oil, silicone fluid, silicone surfactants, volatile hydrocarbon oils, quaternary nitrogen compounds, amine functionalized silicones, conditioning polymers, rheology modifiers, antioxidants, sunscreen active agents, long chain amines from about C10 to C22, long chain fatty amines from about C10 to C22, fatty alcohols, ethoxylated fatty alcohols and phospholipids.

In various embodiments, a composition according to the present invention further comprises at least one skin benefit agent.

In the context of the present invention, a "skin benefit agent" is understood to mean a compound or a mixture of compounds that, upon contact with skin, lends a benefit to the skin compared to skin that was not treated with said compound or mixture of compounds. This benefit can include, for example and without limitation, a moisturizing effect, a skin softening effect, U.V. protection, etc.. Non-limiting examples of classes of skin benefit agents include moisturizing agents, antimicrobial agents, anti-inflammatory agents, antioxidants, UV absorbing agents, additional anti-acne agents, skin pigmentation-inducing agents, and skin pigmentation-blocking agents, and, according to some embodiments, the composition herein described comprises at least one benefit agent selected from the above group of skin benefit agents.

Furthermore, a composition as described herein may comprise at least one component selected from the group consisting of surfactants, solvents, sequestering agents, thickeners, fragrances, pH adjusters, preservatives, dyes, pigments, and opacifiers.

Accordingly, cosmetically or pharmaceutically beneficial ingredients suitable for incorporation in compositions according to the present invention may be selected from, but are not limited to, skin cleansers, cationic, anionic surfactants, non-ionic surfactants, amphoteric surfactants, and zwitterionic surfactants, skin and hair conditioning agents, vitamins, hormones, minerals, plant extracts, anti-inflammatory agents, collagen and elastin synthesis boosters, UVA/UVB sunscreens, concentrates of plant extracts, emollients, moisturizers, skin protectants, humectants, silicones, skin soothing ingredients, antimicrobial agents, antifungal agents, treatment of skin infections and lesions, blood microcirculation improvement, skin redness reduction benefits, additional moisture absorbents, analgesics, skin penetration enhancers, solubilizers, moisturizers, emollients, anesthetics, colorants,

perfumes, preservatives, seeds, broken seed nut shells, silica, clays, beads, luffa particles, polyethylene balls, mica, pH adjusters, processing aids, and combinations thereof.

Non-limiting examples of saccharides suitable for usage according to the present invention include nonionic or cationic saccharides such as agarose, amylopectins, amyloses, arabinans, arabinogalactans, arabinoxylans, carageenans, gum arabic, carboxymethyl guar gum, carboxymethyl(hydroxypropyl) guar gum, hydroxyethyl guar gum, carboxymethyl cellulose, cationic guar gum, cellulose ethers including methyl cellulose, chondroitin, chitins, chitosan, chitosan pyrrolidone carboxylate, chitosan glycolate chitosan lactate, cocodimonium hydroxypropyl oxyethyl cellulose, colominic acid ([poly-N acetyl-neuraminic acid]), corn starch, curdlan, dermatin sulfate, dextrans, furcellarans, dextrans, cross-linked dextrans, dextrin, emulsan, ethyl hydroxyethyl cellulose, flaxseed saccharide (acidic), galactoglucomannans, galactomannans, glucomannans, glycogens, guar gum, hydroxy ethyl starch, hydroxypropyl methyl cellulose, hydroxy ethyl cellulose, hydroxy propyl cellulose, hydroxypropyl starch, hydroxypropylated guar gums, gellan gum, gellan, gum ghatti, gum karaya, gum tragacanth (tragacanthin), heparin, hyaluronic acid, inulin, keratin sulfate, konjac mannan, modified starches, laminarans, laurdimonium hydroxypropyl oxyethyl cellulose, okra gum, oxidized starch, pectic acids, pectin, polydextrose, polyquaternium-4, polyquaternium-10, polyquaternium-28, potato starch, protopectins, psyllium seed gum, pullulan, sodium hyaluronate, starch diethylaminoethyl ether, steardimonium hydroxyethyl cellulose, raffinose, rhamnsan, tapioca starch, whelan, levan, scleroglucan, sodium alginate, stachylose, succinoglycan, wheat starch, xanthan gum, xylans, xyloglucans, and mixtures thereof. Microbial saccharides can be found in Kirk-Othmer Encyclopedia of Chemical Technology, Fourth Edition, Vol. 16, John Wiley and Sons, NY pp. 578-611 (1994), which is incorporated entirely by reference. Complex carbohydrates found in Kirk-Othmer Encyclopedia of Chemical Technology, Fourth Edition, Vol. 4, John Wiley and Sons, NY pp. 930-948, 1995, which is also herein incorporated by reference.

Non-limiting examples of surface-active agents include, without limitation, surfactants, which typically provide deterative functionality to a formulation or act simply as wetting agents. Surface-active agents can generally be categorized as anionic surface-active agents, cationic surface-active agents, nonionic surface-active agents, amphoteric surface-active agents and zwitterionic surface-active agents, dispersion polymers, and combinations thereof.

Anionic surface-active agents useful for employment according to the present invention include, for instance, those disclosed in U.S. Pat. No. 5,573,709, incorporated herein by reference. Particular examples include alkyl and alkyl ether sulfates. Examples of alkyl ether sulfates, which may be used in compositions according to the present invention, are sodium and ammonium salts of lauryl sulfate, lauryl ether sulfate, coconut alkyl triethylene glycol ether sulfate, tallow alkyl triethylene glycol ether sulfate, tallow alkyl hexaoxyethylene sulfate, and combinations thereof. Preferred alkyl ether sulfates are those comprising a mixture of individual compounds, said mixture having an average alkyl chain

length of from about 12 to about 16 carbon atoms and an average degree of ethoxylation of from about 1 to about 6 moles of ethylene oxide.

Another suitable class of anionic surface-active agents is the alkyl sulfuric acid salts. Important examples are the salts of an organic sulfuric acid reaction product of a hydrocarbon of the methane series, including iso-, neo-, and n-paraffins, having about 8 to about 24 carbon atoms, preferably about 12 to about 18 carbon atoms and a sulfonating agent, for example, sulfur trioxide or oleum, obtained according to known sulfonation methods, including bleaching and hydrolysis. Preferred are alkali metal and ammonium sulfated C12-C38 n-paraffins.

Additional synthetic anionic surface-active agents include the olefin sulfonates, the beta-alkyloxy alkane sulfonates, and the reaction products of fatty acids esterified with isethionic acid and neutralized with sodium hydroxide, as well as succinamates. Specific examples of succinamates include disodium N-octadecyl sulfosuccinamate; tetrasodium N-(1,2-dicarboxyethyl)-N-octadecylsulfosuccinamate; diamyl ester of sodium sulfosuccinic acid; dihexyl ester of sodium sulfosuccinic acid; dioctyl esters of sodium sulfosuccinic acid, and combinations thereof.

Preferred anionic surface-active agents for use in compositions of the present invention include ammonium lauryl sulfate, ammonium laureth sulfate, triethylamine lauryl sulfate, triethylamine laureth sulfate, triethanolamine lauryl sulfate, triethanolamine laureth sulfate, monoethanolamine lauryl sulfate, monoethanolamine laureth sulfate, diethanolamine lauryl sulfate, diethanolamine laureth sulfate, lauric monoglyceride sodium sulfate, sodium lauryl sulfate, sodium laureth sulfate, potassium lauryl sulfate, potassium laureth sulfate, sodium lauryl sarcosinate, sodium lauroyl sarcosinate, lauryl sarcosine, cocoyl sarcosine, ammonium cocoyl sulfate, ammonium lauroyl sulfate, sodium cocoyl sulfate, sodium lauroyl sulfate, potassium cocoyl sulfate, potassium lauryl sulfate, triethanolamine lauryl sulfate, triethanolamine lauryl sulfate, monoethanolamine cocoyl sulfate, monoethanolamine lauryl sulfate, sodium tridecyl benzene sulfonate, and sodium dodecyl benzene sulfonate.

Non-limiting examples of suitable amphoteric surface-active agents include derivatives of aliphatic secondary and tertiary amines, in which the aliphatic substituent contains from about 8 to 18 carbon atoms and an anionic water solubilizing group e.g., carboxy, sulfonate, sulfate, phosphate, or phosphonate. Representative examples include sodium 3-dodecyl-aminopropionate, sodium 3-dodecylaminopropane sulfonate, sodium lauryl sarcosinate, N-alkyltaurines such as the one prepared by reacting dodecylamine with sodium isethionate as described in U.S. Pat. No. 2,658,072, N-higher alkyl aspartic acids as described in U.S. Pat. No. 2,438,091, and the products sold under the trade name MIRANOL as described in U.S. Pat. No. 2,528,378. Other sarcosinates and sarcosinate derivatives can be found in the CTFA Cosmetic Ingredient Handbook, Fifth Edition, 1988, page 42 incorporated herein by reference.

Quaternary ammonium compounds can also be used in the herein described compositions as long as they are compatible in the compositions of the invention, wherein the structure is provided in the CTFA Cosmetic Ingredient Handbook, Fifth Edition, 1988, page 40. Cationic surface-active agents generally include, but are not limited to fatty quaternary ammonium compounds containing from about 8 to about 18 carbon atoms. The anion of the quaternary ammonium compound can be a common ion such as chloride, ethosulfate, methosulfate, acetate, bromide, lactate, nitrate, phosphate, or tosylate and mixtures thereof. The long chain alkyl groups can include additional or replaced carbon or hydrogen atoms or ether linkages. Other substitutions on the quaternary nitrogen can be hydrogen, hydrogen, benzyl or short chain alkyl or hydroxyalkyl groups such as methyl, ethyl, hydroxymethyl or hydroxyethyl, hydroxypropyl or combinations thereof.

Non-limiting examples of quaternary ammonium compounds include: Behentrimonium chloride, Cocotrimonium chloride, Cethethyldimonium bromide, Dibehenyldimonium chloride, Dihydrogenated tallow benzylmonium chloride, disoyadimonium chloride, Ditalowdimonium chloride, Hydroxycetyl hydroxyethyl dimonium chloride, Hydroxyethyl Behenamidopropyl dimonium chloride, Hydroxyethyl Cetylmonium chloride, Hydroxyethyl talowdimonium chloride, myristalkonium chloride, PEG-2 Oleammonium chloride, PEG-5 Stearammonium chloride, PEG-15 cocoyl quaternium 4, PEG-2 stearammonium 4, lauryltrimonium chloride; Quaternium-16; Quaternium-18, lauralkonium chloride, olealkmonium chloride, cetylpyridinium chloride, Polyquaternium-5, Polyquaternium-6, Polyquaternium-7, Polyquaternium-10, Polyquaternium-22, Polyquaternium-37, Polyquaternium-39, Polyquaternium-47, cetyl trimonium chloride, dilauryldimonium chloride, cetalkonium chloride, dicetyldimonium chloride, soyatrimonium chloride, stearyl octyl dimonium methosulfate, and mixtures thereof. Other quaternary ammonium compounds are listed in the CTFA Cosmetic Ingredient Handbook, First Edition, on pages 41-42, incorporated herein by reference.

Further suitable for employment in compositions according to the present inventions are long chain (from about C10 to C22) fatty amines and their derivatives. Specific examples include dipalmitylamine, lauramidopropyl dimethylamine, and stearamidopropyl dimethylamine. Fatty alcohols (typically monohydric alcohols), ethoxylated fatty alcohols, and di-tail phospholipids are also suitable and can be used to stabilize emulsion or dispersion forms of the herein described compositions. They also provide a cosmetically acceptable viscosity. Selection of the fatty alcohol is not critical, although those alcohols characterized as having fatty chains of C10 to C32, preferably C14 to C22, which are substantially saturated alkanols will generally be employed. Non-limiting examples include stearyl alcohol, cetyl alcohol, cetostearyl alcohol, myristyl alcohol, behenyl alcohol, arachidic alcohol, isostearyl alcohol, isocetyl alcohol, and combinations thereof. Cetyl alcohol is preferred and may be used alone or in combination with other fatty alcohols, preferably with stearyl alcohol. When used, the fatty alcohol is preferably included in the formulations of this invention at a concentration within the range from about 1 to about 8 weight percent, more preferably about 2 to about 6 weight percent. The fatty alcohols may also be ethoxylated. Specific examples include cetereth-20, steareth-20, steareth-21, and mixtures thereof. Phospholipids such as phosphatidylserine and phosphatidylcholine, and

mixtures thereof may also be included. When used, the fatty alcohol component is included in the formulations at a concentration of about 1 to about 10 weight percent, more preferably about 2 to about 7 weight percent.

Non-limiting of nonionic surface-active agents, which can be used in the context of the present invention, include those broadly defined as compounds produced by the condensation of alkylene oxide groups (hydrophilic in nature) with an organic hydrophobic compound, which may be aliphatic or alkyl aromatic in nature. Examples of preferred classes of nonionic surface-active agents are: the long chain alkanolamides; the polyethylene oxide condensates of alkyl phenols; the condensation product of aliphatic alcohols having from about 8 to about 18 carbon atoms, in either straight chain or branched chain configuration, with ethylene oxide; the long chain tertiary amine oxides; the long chain tertiary phosphine oxides; the long chain dialkyl sulfoxides containing one short chain alkyl or hydroxy alkyl radical of from about 1 to about 3 carbon atoms; and the alkyl polysaccharide (APS) surfactants such as the alkyl polyglycosides; the polyethylene glycol (PEG) glyceryl fatty esters.

Non-limiting examples of zwitterionic surface-active agents include betaines. Examples of betaines useful for employment according to the present invention include the high alkyl betaines, such as coco dimethyl carboxymethyl betaine, cocoamidopropyl betaine, cocobetaine, lauryl amidopropyl betaine, oleyl betaine, lauryl dimethyl carboxymethyl betaine, lauryl dimethyl alphacarboxyethyl betaine, cetyl dimethyl carboxymethyl betaine, lauryl bis-(2-hydroxyethyl) carboxymethyl betaine, stearyl bis-(2-hydroxypropyl) carboxymethyl betaine, oleyl dimethyl gamma-carboxypropyl betaine, and lauryl bis-(2-hydroxypropyl)alpha-carboxyethyl betaine. The sulfobetaines may be represented by coco dimethyl sulfopropyl betaine, stearyl dimethyl sulfopropyl betaine, lauryl dimethyl sulfoethyl betaine, lauryl bis-(2-hydroxyethyl) sulfopropyl betaine and the like; amidobetaines and amidosulfobetaines are also useful.

The anionic, cationic, nonionic, amphoteric or zwitterionic surface-active agents may typically be used in an amount from about 0.1 to 50 wt.-%, preferably from about 0.5 to about 40 wt.-%, more preferably from about 1 to about 20 wt.-%, based on the total weight of the respective composition.

Humectants act as hygroscopic agents, increasing the amount of water absorbed, held and retained. Suitable humectants for the formulations of this invention include, but are not limited to: acetamide MEA, ammonium lactate, chitosan and its derivatives, colloidal oatmeal, galactoarabinan, glucose glutamate, glerecyth-7, glygeryth-12, glycereth-26, glyceryth-31, glycerin, lactamide MEA, lactamide DEA, lactic acid, methyl gluceth-10, methyl gluceth-20, panthenol, propylene glycol, sorbitol, polyethylene glycol, 1,3-butanediol, 1,2,6-hexanetriol, hydrogenated starch hydrolysate, inositol, mannitol, PEG-5 pentaerythritol ether, polyglyceryl sorbitol, xylitol, sucrose, sodium hyaluronate, sodium PCA, and combinations thereof. Glycerin is a particularly preferred humectant. If present, the humectant is present in the composition at concentrations of from about 0.5 independently to about

40 wt.-%, preferably from about 0.5 independently to about 20 wt.-%, and more preferably from about 0.5 independently to about 12 wt.-%, based on the total weight of the respective composition.

Petrolatum or mineral oil components suitable for employment according to the present invention will generally be USP or NF grade. The petrolatum may be white or yellow. The viscosity or consistency grade of petrolatum is not narrowly critical. Petrolatum can be partially replaced with mixtures of hydrocarbon materials, which can be formulated to resemble petrolatum in appearance and consistency. For example, mixtures of petrolatum or mineral oil with different waxes and the like may be combined. Preferred waxes include bayberry wax, candelilla wax, ceresin, jojoba butter, lanolin wax, montan wax, ozokerite, polyglyceryl-3-beeswax, polyglyceryl-6-pentastearate, microcrystalline wax, paraffin wax, isoparaffin, vaseline solid paraffin, squalene, oligomer olefins, beeswax, synthetic candelilla wax, synthetic carnauba, synthetic beeswax and the like may be blended together. Alkylmethyl siloxanes with varying degrees of substitution can be used to increase water retained by the skin. Siloxanes such as stearyl dimethicone, known as 2503 Wax, C30-45 alkyl methicone, known as AMS-C30 wax, and stearoxytrimethylsilane (and) stearyl alcohol, known as 580 Wax, each available from Dow Corning, Midland, Mich., USA. Additional alkyl and phenyl silicones may be employed to enhance moisturizing properties. Resins such as dimethicone (and) trimethylsiloxysilicate or Cyclomethicone (and) Trimethylsiloxysilicate fluid, may be utilized to enhance film formation of skin care products. When used, the petrolatum, wax or hydrocarbon or oil component is included in the formulations at a concentration of about 1 independently to about 20 wt.-%, more preferably about 1 independently to about 12 wt.-%, based on the total weight of the composition. When used, the silicone resins can be included from about 0.1 independently to about 10.0 wt.-%, based on the total weight of the respective composition.

Emollients are defined as agents that help maintain the soft, smooth, and pliable appearance of skin. Emollients function by their ability to remain on the skin surface or in the stratum corneum. Composition according to the present invention may include, for instance and without limitation, fatty ester emollients, which are listed in the International Cosmetic Ingredient Dictionary, Eighth Edition, 2000, p. 1768 to 1773. Specific examples of suitable fatty esters for use in the formulation of this invention include isopropyl myristate, isopropyl palmitate, caprylic/capric triglycerides, cetyl lactate, cetyl palmitate, hydrogenated castor oil, glyceryl esters, hydroxycetyl isostearate, hydroxy cetyl phosphate, isopropyl isostearate, isostearyl isostearate, diisopropyl sebacate, PPG-5-Ceteth-20, 2-ethylhexyl isononoate, 2-ethylhexyl stearate, C12 to C16 fatty alcohol lactate, isopropyl lanolate, 2-ethyl-hexyl salicylate, and mixtures thereof. The presently preferred fatty esters are isopropyl myristate, isopropyl palmitate, PPG-5-Ceteth-20, and caprylic/capric triglycerides. When used, the fatty ester emollient is preferably included in the formulations of this invention at a concentration of about 1 to about 8 wt.-%, more preferably about 2 to about 5 wt.-%, based on the total weight of the respective formulation.

Further suitable for employment in the context of the present invention are silicone compounds. Preferably, the viscosity of the silicone component is from about 0.5 to about 12,500 cps. Examples of suitable materials are dimethylpolysiloxane, diethylpolysiloxane, dimethylpolysiloxane-diphenylpolysiloxane, cyclomethicone, trimethylpolysiloxane, diphenylpolysiloxane, and mixtures thereof. Dimethicone, a dimethylpolysiloxane endblocked with trimethyl units, is one preferred example. Dimethicone having a viscosity between 50 and 1,000 cps is particularly preferred. When used, the silicone oils are preferably included in the formulations of this invention at a concentration of 0.1 to 5 wt.-%, more preferably 1 to 2 wt.-%, based on the total weight of the respective formulation.

A composition, as herein described, may further contain volatile and non-volatile silicone oils or fluids. The silicone compounds can be either linear or cyclic polydimethylsiloxanes with a viscosity from about 0.5 to about 100 centistokes. The most preferred linear polydimethylsiloxane compounds have a range from about 0.5 to about 50 centistokes. One example of a linear, low molecular weight, volatile polydimethylsiloxane is octamethyltrisiloxane 200 fluid having a viscosity of about 1 centistoke. When used, the silicone oils are preferably included in the formulations of this invention at a concentration of 0.1 to 30 wt.-%, more preferably 1 to 20 wt.-%, based on the total weight of the respective formulation.

Further ingredients suitable for incorporation in compositions according to the present invention are volatile, cyclic, low molecular weight polydimethylsiloxanes (cyclomethicones). Preferred cyclic volatile siloxanes may be selected from polydimethyl cyclosiloxanes having an average repeat unit of 4 to 6, and a viscosity from about 2.0 to about 7.0 centistokes, and mixtures thereof. Preferred cyclomethicones are available from Dow Corning, Midland, Mich., and from General Electric, Waterford, N.Y., USA. When used, the silicone oils may be included in the formulations of this invention at a concentration of 0.1 to 30 wt.-%, more preferably 1 to 20 wt.-%, based on the respective total weight of a formulation according to the present invention.

Silicone surfactants or emulsifiers with polyoxyethylene or polyoxypropylene side chains may also be used in compositions of the present invention. Preferred examples include dimethicone copolyols and 5225C Formulation Aids, available from Dow Corning, Midland, Mich., USA and Silicone SF-1528, available from General Electric, Waterford, N.Y., USA. The side chains may also include alkyl groups such as lauryl or cetyl. Preferred are lauryl methicone copolyol. 5200 Formulation Aid, and cetyl dimethicone copolyol, known as Abil EM-90, available from Goldschmidt Chemical Corporation, Hopewell, Va. Also preferred is lauryl dimethicone, known as Belsil LDM 3107 VP, available from Wacker-Chemie, München, Germany. When used, the silicone surfactants are preferably included in the formulations of this invention at a concentration of 0.1 to 30 weight percent, more preferably 1 to 15 weight percent. Amine functional silicones and emulsions may be utilized in the present invention. Preferred examples include Dow Corning 8220, Dow Corning 939, Dow Corning 949, Dow Corning 2-8194, all available from Dow Corning, Midland, Mich., USA. Also preferred is Silicone SM 253 available from General Electric, Waterford, N.Y., USA. When used, the amine functional silicones

may be included in the formulations of this invention at concentrations in the range of 0.1 to 5 wt.-%, more preferably in the range of 0.1 to 2.0 wt.-%.

Further suitable ingredients are volatile hydrocarbon oils comprising from about C6 to C22 atoms. A non-limiting example of preferred volatile hydrocarbons is an aliphatic hydrocarbon having a chain length from about C6 to C16 carbon atoms. An example of such a compound is isohexadecane, sold under the tradename Permethyl 101A, available from Presperse, South Plainfield, N.J., USA. Another example of a preferred volatile hydrocarbon is C12 to C14 isoparaffin, marketed under the tradename Isopar M, available from Exxon, Baytown, Tex., USA. When used, the volatile hydrocarbons are preferably included in the formulations of this invention at a concentration in the range of about 0.1 independently to 30 wt.-%, more preferably about 1 independently to 20 wt.-%.

The herein disclosed compositions may further contain cationic and ampholytic conditioning polymers. Examples of such include, but are not limited to, those listed by the International Cosmetic Ingredient Dictionary published by the Cosmetic, Toiletry, and Fragrance Association (CTFA), 1110 17 Street, N.W., Suite 300, Washington, D.C. 20036. General, non-limiting examples include quaternary derivatives of cellulose ethers, quaternary derivatives of guar, homopolymers and copolymers of DADMAC, homopolymers and copolymers of MAPTAC and quaternary derivatives of starches. Specific examples, using the CTFA designation, include, but are not limited to Polyquaternium-10, Guar hydroxypropyltrimonium chloride, Starch hydroxypropyltrimonium chloride, Polyquaternium-4, Polyquaternium-5, Polyquaternium-6, Polyquaternium-7, Polyquaternium-14, Polyquaternium-15, Polyquaternium-22, Polyquaternium-24, Polyquaternium-28, Polyquaternium-32, Polyquaternium-33, Polyquaternium-36, Polyquaternium-37, Polyquaternium-39, Polyquaternium-45, Polyquaternium-47 and polymethacrylamidopropyltrimonium chloride, and mixtures thereof. When used, the conditioning polymers are preferably included in the herein described compositions at a concentration in the range of about 0.1 independently to 10 wt.-%, preferably about 0.2 independently to 6 wt.-% and most preferably about 0.2 independently to 5 wt.-%.

Another type of ingredients suitable for employment according to the present invention are rheological modifiers. The rheological modifiers that can be used in this invention include, but are not limited to, high molecular weight crosslinked homopolymers of acrylic acid, and Acrylates/C10-30 Alkyl Acrylate Crosspolymer, such as the Carbopol and Pemulen series, both available from B. F. Goodrich, Akron, Ohio, USA; anionic acrylate polymers such as Salcare and cationic acrylate polymers such as Salcare SC96, available from Ciba Specialties, High Point, N.C., USA; Acrylamidopropyltrimonium chloride/acrylamide; Hydroxyethyl methacrylates polymers, Steareth-10 Allyl Ether/Acrylate Copolymer; Acrylates/Beheneth-25 Metacrylate Copolymer, known as Aculyn, available from International Specialties, Wayne, N.J., USA; Glyceryl Polymethacrylate, Acrylates/Steareth-20 Methacrylate Copolymer; bentonite; gums such as alginates, carageenans, gum acacia, gum arabic, gum ghatti, gum karaya, gum tragacanth, guar gum; guar hydroxypropyltrimonium chloride, xanthan gum or gellan gum; cellulose derivatives such as sodium carboxymethyl cellulose, hydroxyethyl

cellulose, hydroxymethyl carboxyethyl cellulose, hydroxymethyl carboxypropyl cellulose, ethyl cellulose, sulfated cellulose, hydroxypropyl cellulose, methyl cellulose, hydroxypropylmethyl cellulose, microcrystalline cellulose; agar; pectin; gelatin; starch and its derivatives; chitosan and its derivatives such as hydroxyethyl chitosan; polyvinyl alcohol, PVM/MA copolymer, PVM/MA decadiene crosspolymer, poly(ethylene oxide) based thickeners, sodium carbomer, and mixtures thereof. When used, the rheology modifiers are preferably included in the composition according to the present invention at a concentration in the range of about 0.01 independently to 12 wt.-%, preferably about 0.05 independently to 10 wt.-%, and most preferably about 0.1 independently to 6 wt.-%.

A composition, as herein disclosed and described, may further include one or more antioxidants, which may be selected from, but are not limited to the group consisting of ascorbic acid, BHT, BHA, erythorbic acid, bisulfite, thioglycolate, tocopherol, sodium metabisulfite, vitamin E acetate, and ascorbyl palmitate. The antioxidants may be present in the herein described compositions at a concentration in the range of about 0.01 independently to 5 wt.-%, preferably about 0.1 independently to 3 wt.-%, and most preferably about 0.2 independently to 2 wt.-%, based on the total weight of a respective composition.

Examples of sunscreen active agents suitable for incorporation in compositions as herein described include, but are not limited to octyl methoxycinnamate (ethylhexyl p-methoxycinnamate), octyl salicylate oxybenzone (benzophenone-3), benzophenone-4, menthyl anthranilate, dioxybenzone, aminobenzoic acid, amyl dimethyl PABA, diethanolamine p-methoxy cinnamate, ethyl 4-bis (hydroxypropyl) aminobenzoate, 2-ethylhexy 1-2-cyano-3,3-diphenylacrylate, homomenthyl salicylate, glyceryl aminobenzoate, dihydroxyacetone, octyl dimethyl PABA, 2-phenylbenzimidazole-5-sulfonic acid, triethanolamine salicylate, zinc oxide, titanium oxide, and mixtures thereof. The amount of sunscreen used in a composition according to the present invention will vary depending on the specific UV absorption wavelength(s) of the specific sunscreen active(s) used and may, for instance, be in the range of about 0.1 independently to 10 wt.-%, preferably about 2 independently to 8 wt.-%.

Non-limiting example of preservatives useful in the context of the present invention include, but are not limited to 1,2-dibromo-2,4-dicyano butane (Methyldibromo Glutaronitrile, known as MERGUARD, Nalco Chemical Company, Naperville, Ill., USA), benzyl alcohol, imidazolidinyl urea, 1,3-bis (hydroxymethyl)-5,5-dimethyl-2,3-imidazolidinedione (e.g., DMDM Hydantoin, known as GLYDANT, Lonza, Fairlawn, N.J., USA.), methylchloroisothiazolinone and methylisothiazolinone (e.g., Kathon, Rohm & Haas Co., Philadelphia, Pa., USA), methyl paraben, propyl paraben, phenoxyethanol, sodium benzoate, and mixtures thereof.

Non-limiting examples of further ingredients that may advantageously find application in the context of the present invention include, but are not limited to buffering agents, fragrance ingredients, chelating agents, color additives or dyestuffs which can serve to color the composition itself or keratin,

sequestering agents, softeners, foam synergistic agents, foam stabilizers, sun filters and peptizing agents.

The surface of pigments, such titanium dioxide, zinc oxide, talc, calcium carbonate or kaolin, can be treated with the unsaturated quaternary ammonium compounds described herein and then used in a composition according to the present invention. Accordingly treated pigments are more effective as sunscreen actives and may further be used in color cosmetics such as make up and mascara.

The herein described compositions can be presented in various forms. Examples of such forms include, but are not limited a solution, liquid, cream, emulsion, dispersion, gel, thickening lotion.

Compositions according to the present invention may contain water and also any cosmetically and/or pharmaceutically acceptable solvent. Examples of acceptable solvents include, but are not limited to monoalcohols, such as alkanols having 1 to 8 carbon atoms (like ethanol, isopropanol, benzyl alcohol and phenylethyl alcohol) polyalcohols, such as alkylene glycols (like glycerine, ethylene glycol and propylene glycol) and glycol ethers, such as mono-, di- and tri-ethylene glycol monoalkyl ethers, for example ethylene glycol monomethyl ether and diethylene glycol monomethyl ether, used singly or in a mixture. These solvents can be present in proportions of up to as much as 70 wt.-%, for example from about 0.1 to 70 wt.-%, based on the total weight of the respective composition.

Compositions as herein described can also be packaged as an aerosol, in which case it can be applied either in the form of an aerosol spray or in the form of an aerosol foam. As the propellant gas for these aerosols, in particular but without limitation, dimethyl ether, carbon dioxide, nitrogen, nitrous oxide, air and volatile hydrocarbons, such as butane, isobutane, and propane, may be mentioned.

Further included may be electrolytes, such as aluminum chlorohydrate, alkali metal salts, e.g., sodium, potassium or lithium salts, these salts preferably being halides, such as the chloride or bromide, and the sulfate, or salts with organic acids, such as the acetates or lactates, and also alkaline earth metal salts, preferably the carbonates, silicates, nitrates, acetates, gluconates, pantothenates and lactates of calcium, magnesium and/or strontium, and combinations thereof.

Compositions for treating skin that contain at least one compound according to Chemical Formula (I), as herein disclosed and described, and at least one pharmaceutically or cosmetically acceptable carrier include leave-on or rinse-off skin care products such as lotions, hand/body creams, shaving gels or shaving creams, body washes, sunscreens, liquid soaps, deodorants, antiperspirants, suntan lotions, after sun gels, bubble baths, hand or mechanical dishwashing compositions, and the like. Any components of the herein described compositions must in general be safe for application to the human skin and must be compatible with the other components of the formulation. Selection of these components is generally within the skill of the art. The skin care compositions may also contain other

conventional additives employed in cosmetic skin care formulations. Such additives include aesthetic enhancers, fragrance oils, dyes and medicaments such as menthol and the like.

Thus, according to various embodiments, a composition, as herein described and defined is a skin cleanser, toner, serum, lotion, cream, emulsion, gel, make-up composition (foundation, make-up, powder), skin mask, hair mask, shampoo, or conditioner.

The skin care compositions that contain sebum reducing agents of the present invention may be prepared as oil-in-water, water-in-oil emulsions, triple emulsions, or dispersions.

Preferred oil-in-water emulsions are prepared by first forming an aqueous mixture of the water-soluble components, e.g. unsaturated quaternary ammonium compounds, humectants, water-soluble preservatives, followed by adding water-insoluble components. The water-insoluble components include the emulsifier, water-insoluble preservatives, petrolatum or mineral oil component, fatty alcohol component, fatty ester emollient, and silicone oil component. The input of mixing energy will be high and will be maintained for a time sufficient to form a water-in-oil emulsion having a smooth appearance (indicating the presence of relatively small micelles in the emulsion). Preferred dispersions are generally prepared by forming an aqueous mixture of the water-soluble components, followed by addition of thickener with suspension power for water-insoluble materials.

Compositions that contain at least one lipid production-decreasing compound, i.e. at least one compound according to Chemical Formula (I), as herein defined above, for treating hair include bath preparations such as bubble baths, soaps, and oils, shampoos, conditioners, hair bleaches, hair coloring preparations, temporary and permanent hair colors, color conditioners, hair lighteners, coloring and non-coloring hair rinses, hair tints, hair wave sets, permanent waves, curling, hair straighteners, hair grooming aids, hair tonics, hair dressings and oxidative products. The compounds of the present invention may also be utilized in styling type leave-in products such as gels, mousses, spritzes, styling creams, styling waxes, pomades, balms, and the like.

In the case of cleansing formulations such as a shampoo for washing the hair, or a liquid hand soap, or shower gel, compositions according to the present invention generally contain anionic, cationic, nonionic, zwitterionic and/or amphoteric surface-active agents typically in an amount from about 3 independently to about 50 wt.-%, preferably from about 3 independently to about 20 wt.-%, and the pH of such compositions is generally in the range from about 3 independently to about 10.

Rinsing lotions according to the present invention, to be applied mainly before or after shampooing, are typically aqueous or aqueous-alcoholic solutions, emulsions, thickened lotions or gels. If the compositions are presented in the form of an emulsion, they can be nonionic, anionic or cationic. The nonionic emulsions consist mainly of a mixture of oil and/or a fatty alcohol with a polyoxyethyleneated

alcohol, such as polyoxyethyleneated stearyl or cetyl/stearyl alcohol, and cationic surface-active agents can be added to these compositions. The anionic emulsions are formed essentially from soap.

If the compositions according to the present invention are presented in the form of a thickened lotion or a gel, they contain thickeners in the presence or absence of a solvent. Thickeners, which can be used, may be selected from resins, Carbopol-type acrylic acid thickeners available from B.F. Goodrich; xanthan gums; sodium alginates; gum arabic; cellulose derivatives and poly-(ethylene oxide) based thickeners. It is also possible to achieve thickening by means of a mixture of polyethylene glycol stearate or distearate, or by means of a mixture of a phosphoric acid ester and an amide. The concentration of thickener is generally in the range of about 0.05 to 15 wt.-%, based on the total weight of the respective composition.

In the case of hair fixatives, the compositions of the present invention may also contain one or more hair fixative polymers. When present, hair fixative polymers may be present in an amount of about 0.25 to about 10 wt.-%, based on the total weight of the respective composition. For instance, hair fixative resins may be selected from the group consisting of acrylamide copolymer, acrylamide/sodium acrylate copolymer, acrylate/ammonium methacrylate copolymer, an acrylate copolymer, an acrylic/acrylate copolymer, adipic acid/dimethylaminohydroxypropyl diethylenetriamine copolymer, adipic acid/epoxypropyl diethylenetriamine copolymer, allyl stearate/VA copolymer, aminoethylacrylate phosphate/acrylate copolymer, an ammonium acrylate copolymer, an ammonium vinyl acetate/acrylate copolymer, an AMP acrylate/diacetoneacrylamide copolymer, an AMPD acrylate/diacetoneacrylamide copolymer, butyl ester of ethylene/maleic anhydride copolymer, butyl ester of PVM/MA copolymer, calcium/sodium PVM/MA copolymer, corn starch/acrylamide/sodium acrylate copolymer, diethylene glycolamine/epichlorohydrin/piperazine-copolymer, dodecanedioic acid/cetearyl alcohol/glycol copolymer, ethyl ester of PVM/MA copolymer, isopropyl ester of PVM/MA copolymer, karaya gum, a methacryloyl ethyl betaine/methacrylate copolymer, an octylacrylamide/acrylate/butylaminoethyl methacrylate copolymer, an octylacrylamide/acrylate copolymer, phthalic anhydride/glycerin/glycidyl decanoate copolymer, a phthalic/trimellitic/glycol copolymer, polyacrylamide, polyacrylamidomethylpropane sulfonic acid, polybutylene terephthalate, polyethylacrylate, polyethylene, polyquaternium-1, polyquaternium-2, polyquaternium-4, polyquaternium-5, polyquaternium-6, polyquaternium-7, polyquaternium-8, polyquaternium-9, polyquaternium-10, polyquaternium-11, polyquaternium-12, polyquaternium-13, polyquaternium-14, polyquaternium-15, polyquaternium-39, polyquaternium-47, polyvinyl acetate, polyvinyl butyral, polyvinyl imidazolinium acetate, polyvinyl methyl ether, PVM/MA copolymer, PVP, PVP/dimethylaminoethylmethacrylate copolymer, PVP/eicosene copolymer, PVP/ethyl methacrylate/methacrylic acid copolymer, PVP/hexadecene copolymer, PVP/VA copolymer, PVP/vinyl acetate/itaconic acid copolymer, shellac, sodium acrylates copolymer, sodium acrylates/Acrylnitrogens copolymer, sodium acrylate/vinyl alcohol copolymer, sodium carrageenan, starch diethylaminoethyl ether, stearylvinyl ether/maleic anhydride copolymer, sucrose benzoate/sucrose acetate isobutyrate/butyl benzyl phthalate copolymer, sucrose benzoate/sucrose

acetate isobutyrate/butyl benzyl phthalate/methyl methacrylate copolymer, sucrose benzoate/sucrose acetate isobutyrate copolymer, a vinyl acetate/crotonate copolymer, vinyl acetate/crotonic acid copolymer, vinyl acetate/crotonic acid/methacryloxybenzophenone-1 copolymer, vinyl acetate/crotonic acid/vinyl neodecanoate copolymer, and mixtures thereof. Synthetic polymers used for creating styling aids are described in "The History of Polymers in Haircare," Cosmetics and Toiletries, 103 (1988), incorporated herein by reference. Other synthetic polymers that may be used are referenced in the CTFA Dictionary, Fifth Edition, 2000.

The pharmaceutically or cosmetically acceptable carrier contained in the compositions according to the present invention may be varied depending on the type of the formulation. Generally, and according to various embodiments of the present invention, a cosmetic composition according to the present invention comprises at least one cosmetically acceptable carrier, and a pharmaceutical composition according to the present invention comprises at least one pharmaceutically acceptable carrier. For example, formulations in the form of ointments, pastes, creams or gels may comprise animal and vegetable fats, waxes, paraffins, starch, tragacanth, cellulose derivatives, polyethylene glycols, silicones, bentonites, silica, talc, zinc oxide, or mixtures of these ingredients.

In the case of formulations in the form of powders or sprays, lactose, talc, silica, aluminum hydroxide, calcium silicate, polyamide powder, and mixtures of the aforementioned may be mentioned. Spray may additionally comprise the customary propellants, for example, chlorofluorohydrocarbons, propane, butane, diethyl ether, or dimethyl ether.

For solution- and emulsion-type formulations according to the present invention, solvents, solubilizers and emulsifiers, for example water, ethanol, isopropanol, ethyl carbonate, ethyl acetate, benzyl alcohol, benzyl benzoate, propylene glycol, 1,3-butyleneglycol, oils, in particular cottonseed oil, groundnut oil, maize germ oil, olive oil, castor oil and sesame seed oil, glycerol fatty esters, polyethylene glycol and fatty acid esters of sorbitan, and mixtures of the aforementioned may be mentioned.

Suspension-type formulations according to the present invention may comprise liquid diluents, for example water, ethanol or propylene glycol, suspending agents, for example ethoxylated isostearyl alcohols, polyoxyethylene sorbitol esters and polyoxyethylene sorbitan esters, microcrystalline cellulose, aluminum metahydroxide, bentonite, agar and tragacanth, or mixtures of the aforementioned.

Cleansing compositions according to the present invention may comprise aliphatic alcohol sulfate, aliphatic alcohol ether sulfate, sulfosuccinate monoester, isothionate, imidazolium derivatives, methyltaurate, sarcocinate, fatty acid amide ether sulfate, alkyl amido betain, aliphatic alcohol, fatty acid glyceride, fatty acid diethanolamide, vegetable oil, lanoline derivatives, ethoxylated glycerol fatty acid ester, or mixtures of the aforementioned.

Additional antioxidant ingredients can be selected from, without limitation, Ascorbic acid, Ascorbic acid derivatives, Glucosamine ascorbate, Arginine ascorbate, Lysine ascorbate, Glutathione ascorbate, Nicotinamide ascorbate, Niacin ascorbate, Allantoin ascorbate, Creatine ascorbate, Creatinine ascorbate, Chondroitin ascorbate, Chitosan ascorbate, DNA Ascorbate, Carnosine ascorbate, Vitamin E, various Vitamin E derivatives, Tocotrienol, Rutin, Quercetin, Hesperedin (*Citrus sinensis*), Diosmin (*Citrus sinensis*), Mangiferin (*Mangifera indica*), Mangostin (*Garcinia mangostana*), Cyanidin (*Vaccinium myrtillus*), Astaxanthin (*Haematococcus algae*), Lutein (*Tagetes patula*), Lycopene (*Lycopersicum esculentum*), Resveratrol (*Polygonum cuspidatum*), Tetrahydrocurcumin (*Curcuma longa*), Rosmarinic acid (*Rosmarinus officinalis*), Hypericin (*Hypericum perforatum*), Ellagic acid (*Punica granatum*), Chlorogenic acid (*Vaccinium vulgaris*), Oleuropein (*Olea europaea*), α -Lipoic acid, Niacinamide lipoate, Glutathione, Andrographolide (*Andrographis paniculata*), Carnosine, Niacinamide, *Potentilla erecta* extract, Polyphenols, Grapeseed extract, Pycnogenol (Pine Bark extract), Pyridoxine, Magnolol, Honokiol, Paeonol, Resacetophenone, Quinacetophenone, arbutin, kojic acid, and combinations thereof.

Furthermore, ingredients for improving blood micro-circulation can be added to compositions according to the present invention. Suitabel, non-limiting examples may be selected from Horse Chestnut Extract (*Aesculus hippocastanum* extract)), Esculin, Escin, Yohimbine, Capsicum Oleoresin, Capsaicin, Niacin, Niacin Esters, Methyl Nicotinate, Benzyl Nicotinate, Ruscogenins (Butchers Broom extract; *Ruscus aculeatus* extract), Diosgenin (*Trigonella foenumgraecum*, Fenugreek), *Emblica* extract (*Phyllanthus emblica* extract), Asiaticoside (*Centella asiatica* extract), *Boswellia* Extract (*Boswellia serrata*), Ginger Root Extract (*Zingiber Officinalis*), Piperine, Vitamin K, Melilot (*Melilotus officinalis* extract), Glycyrrhetic acid, Ursolic acid, Sericoside (*Terminalia sericea* extract), Darutoside (*Siegesbeckia orientalis* extract), *Amni visnaga* extract, extract of Red Vine (*Vitis Vinifera*) leaves, apigenin, phytosan, luteolin, and combinations of the aforementioned.

Anti-inflammatory ingredients suitable for use in the context of the present invention may be selected from the group consisting of Cyclo-oxygenase (for example, COX-1 or COX-2) or Lipoxygenase (for example, LOX-5) enzyme inhibitors such as Ascorbic acid, Ascorbic acid derivatives, Vitamin E, Vitamin E derivatives, Tocotrienol, Rutin, Quercetin, Hesperedin (*Citrus sinensis*), Diosmin (*Citrus sinensis*), Mangiferin (*Mangifera indica*), Mangostin (*Garcinia mangostana*), Cyanidin (*Vaccinium myrtillus*), Astaxanthin (*Haematococcus algae*), Lutein (*Tagetes patula*), Lycopene (*Lycopersicum esculentum*), Resveratrol (*Polygonum cuspidatum*), Tetrahydrocurcumin (*Curcuma longa*), Rosmarinic acid (*Rosmarinus officinalis*), Hypericin (*Hypericum perforatum*), Ellagic acid (*Punica granatum*), Chlorogenic acid (*Vaccinium vulgaris*), Oleuropein (*Olea europaea*), α -Lipoic acid, Glutathione, Andrographolide, Grapeseed extract, Green Tea Extract, Polyphenols, Pycnogenol (Pine Bark extract), White Tea extract, Black Tea extract, (*Andrographis paniculata*), Carnosine, Niacinamide, and *Emblica* extract. Anti-inflammatory composition can additionally be selected from, but not limited to, Horse Chestnut Extract (*Aesculus hippocastanum* extract)), Esculin, Escin,

Yohimbine, Capsicum Oleoresin, Capsaicin, Niacin, Niacin Esters, Methyl Nicotinate, Benzyl Nicotinate, Ruscogenins (Butchers Broom extract; *Ruscus aculeatus* extract), Diosgenin (*Trigonella foenumgraecum*, Fenugreek), *Emblica* extract (*Phyllanthus emblica* extract), Asiaticoside (*Centella asiatica* extract), *Boswellia* Extract (*Boswellia serrata*), Sericoside, Visnadine, Thiocolchicoside, Grapeseed Extract, Ginger Root Extract (*Zingiber Officianalis*), Piperine, Vitamin K, Melilot (*Melilotus officinalis* extract), Glycyrrhetic acid, Ursolic acid, Sericoside (*Terminalia sericea* extract), Darutoside (*Siegesbeckia orientalis* extract), Amni visnaga extract, extract of Red Vine (*Vitis-Vinifera*) leaves, apigenin, phytosan, luteolin. Usage of mixtures of the aforementioned is also possible.

Furthermore, certain divalent metal ions can be added to compositions according to the present invention, examples of which include zinc, copper, manganese, vanadium, chromium, cobalt, and iron.

The application of sebum reducing agents of the present invention can be in several areas of consumer interest, some of which include control of excess facial oil associated with acne, control of excess oil on scalp associated with dandruff, and control of excess body and underarm oil associated with body and underarm malodor. Generally, compositions according to the present invention, as defined and described above, are for decreasing lipid production in sebocytes.

A composition, as herein described, is manufactured using usual and known methods and processes, depending on form and intended end-use of the respective composition.

In a further aspect, the present invention relates to the use of a composition, as herein described above, for decreasing lipid production in sebocytes.

In a further aspect, the present invention also relates to a cosmetic method for decreasing lipid production in sebocytes or in the skin of an individual in need thereof, comprising contacting said sebocyte or skin with an effective amount, i.e. a lipid production-decreasing amount, as defined herein, of at least one compound according to Chemical Formula (I), as defined herein, or with at least one composition according to the present invention, as herein defined above.

The term "contacting", as used herein, is meant to refer to the exposing of a sebocyte or the skin of an individual with an amount effective to bring about the desired effect, i.e. with a lipid production-decreasing amount, as herein defined, of at least one compound according to Chemical Formula (I) or at least one composition according to the present invention. In line with the above disclosure, the term "exposing" is meant to refer to the application of at least one compound according to Chemical Formula (I), as herein defined and described, or of at least one composition, as herein defined and described, for instance in the form of a leave-on or rinse-off product composition, to said sebocytes or skin of an individual.

Generally, the uses, methods and compositions of the present invention thus relate to topical application of at least one compound according to Chemical Formula (I) or at least one composition, as herein described above, so as to treat, reverse, ameliorate and/or prevent signs of lipid overproduction on or within the skin.

The uses, methods and compositions of the present invention, intended for decreasing lipid production in sebocytes and/or in the skin of an individual in need thereof, may comprise the topical application of at least one compound according to Chemical Formula (I) or at least one composition, as herein described above, over an affected area for a period of time sufficient to reduce, ameliorate, reverse or prevent dermatological signs of lipid over-production. Areas affected by lipid overproduction include, but are not limited to oily areas of the skin, e.g., oily facial skin (especially in T-zone-forehead, nose, and chin) or an area of the scalp, as well as non-facial areas, such as the chest, neck, shoulders, and/or back.

Without wishing to be bound by theory, it is believed that the compounds according to Chemical Formula (I) of the present invention, may provide such benefits through one or more activities including, but not limited to, decreasing triglyceride, wax ester, squalene and cholesterol levels in sebocytes, such as by bringing about one of more of a decrease in intracellular lipid and/or triglyceride, wax ester, squalene and cholesterol production, storage, and/or accumulation; and an increase in fatty acid oxidation, degradation and/or lipolysis.

Generally, the improvement in the condition and/or aesthetic appearance is selected from the group consisting of: reducing lipid production by sebaceous glands; reducing triglyceride synthesis; reducing wax ester synthesis; reducing squalene synthesis; reducing fatty acid synthesis; preventing and/or improving conditions related to skin associated with nonselective or partially selective FAS stimulators/up regulators, nonselective or partially selective acyl-CoA wax alcohol acyltransferase 1 (AWAT1) stimulators/up regulators, nonselective or partially selective squalene synthase (SQS) stimulators/up regulators; preventing, ameliorating or treating oily skin; preventing, ameliorating or treating oily hair; preventing, ameliorating or treating oily scalp; preventing, ameliorating or treating enlarged pores; preventing, ameliorating, or treating acne-prone skin; preventing, ameliorating or treating body odors associated with excess sebum production; and any combinations thereof.

The compounds, compositions, uses and methods of the present invention provide an anti-oil/sebum effect so as to produce a visible or palpable improvement in skin affected by excess sebum, i.e. lipid overproduction in sebocytes. Such improvements include, without limitation, restoration of a matte finish to the skin; an evening of skin type; reduction in oily/greasy feel to skin and/or hair; reduction in the incidence of dandruff; reduction in the incidence of blocked/clogged pores; reduction in the incidence of comedones; reduction in the incidence of acne lesions; reduction in the area over-producing lipids; reduction in thickness of skin affected by over-production of lipids.

In accordance with the herein described methods and uses, an effective amount of a compound according to Chemical Formula (I) may be applied to exposed areas of the skin, such as in the form of a composition, as herein defined and described, and, if necessary, may then be spread over and/or rubbed into the skin using the hand or fingers or a suitable device. The compound or composition comprising the same may be applied as frequently as needed to achieve the desired effects. Thus, one will appreciate that the composition may be applied daily, according to various embodiment multiple times per day, i.e. 2 or more times per day, such as at least three times per day, when an individual is experiencing the appearance of excess sebum to provide immediate relief and/or, eventually, maintain the desired complexion.

The compounds and/or compositions may be applied proactively and/or preventively to areas of the skin known to exhibit sebum overproduction. Such areas may include any area on the individual's skin he/she feels exhibits or in his/her personal experience exhibits over-production of lipids.

Further, the methods, compounds, and compositions of the present invention may be used to prevent and/or reduce the incidence of various conditions such as acne and/or dandruff associated with hyper-seborrheic skin. A reduction in the incidence of these conditions includes, but is not limited to, a reduction in the frequency, a reduction in the severity, and/or reduction of the area over which such conditions occur. Thus, in practice, the compounds and/or compositions of the present invention are applied to skin in need of treatment, that is, skin which suffers from a deficiency or loss in any of the foregoing attributes, or which would otherwise benefit from improvement in any of the foregoing skin attributes.

According to various embodiments, the compounds and/or composition of the present invention are intended for use in non-therapeutic treatment methods. In some embodiments, the compounds and/or compositions are intended to be rubbed, poured, sprinkled, or sprayed on, or otherwise applied to the human body for cleansing, beautifying, attractiveness-promoting, or appearance-altering purposes.

The following examples are given to illustrate the present invention. Because these examples are given for illustrative purposes only, the invention should not be deemed limited thereto.

EXAMPLES

Example 1: Lipid-production lowering efficiency of pure phenol compounds

The amount of lipid produced by sebocytes was determined by applying a fluorescent lipid dye to an Asian primary sebocyte cell line, and the fluorescent signal was measured using a fluorescent plate reader and flow cytometer in separate experiments. The fluorescent intensity for each compound treatment was compared against vehicle (DMSO) control treatment.

Testing protocol:

A sebocyte cell line derived from an Asian female donor was used for all experiments. For the plate reader experiment, 30,000 sebocytes were seeded per 0.32 cm² along with the respective compound and incubated at 37 °C and 5 % CO₂ for 72 hours. After 3 days incubation, the media was discarded. The cells were fixed in 4 % paraformaldehyde for 20 minutes, then rinsed with an equal amount of PBS. A solution of Hoechst and 3 % AdipoRed was used to stain for DNA content and neutral lipid respectively. Cells were incubated in the staining solution for 20 minutes at 37 °C and 5 % CO₂. Cells were rinsed once with PBS, and fluorescence intensity for Hoechst and AdipoRed was measured by a fluorescence plate reader at excitation/emission wavelength of 350/461 nm and 485/572 nm, respectively.

For the flow cytometer experiment, 60,000 sebocytes were seeded per 1.9 cm² along with the respective compound and incubated in 37 °C and 5 % CO₂ for 72 hours. After 3 days incubation, the media was discarded. The cells were stained with 0.06% AdipoRed dye for 20 minutes at 37 °C and 5% CO₂. Subsequently, the dye was discarded and the cells were collected using 0.125 % Trypsin. An equal volume of flow cytometry buffer consisting of DMEM without phenol red, 10 % fetal bovine serum and 4 % paraformaldehyde was added. Fluorescence intensity for AdipoRed was measured using a flow cytometer with laser and filter settings for Alexa 488.

The results obtained for each experiment show that both bakuchiol and pterostilbene reduce lipid production in primary sebocyte line, as determined by both the fluorescent plate reader and flow cytometer measurements. The results of the respective measurements are depicted in Figures 1 and 2.

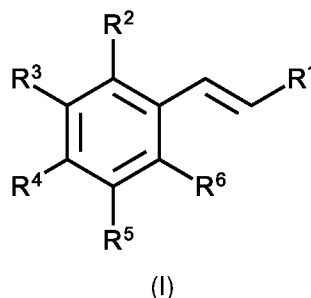
All documents cited herein, are hereby incorporated by reference in their entirety.

The inventions illustratively described herein may suitably be practiced in the absence of any element or elements, limitation or limitations, not specifically disclosed herein. Thus, for example, the terms "comprising", "including", "containing", etc. shall be read expansively and without limitation. Additionally, the terms and expressions employed herein have been used as terms of description and not of limitation, and there is no intention in the use of such terms and expressions of excluding any

equivalents of the features shown and described or portions thereof, but it is recognized that various modifications are possible within the scope of the invention claimed. Thus, it should be understood that although the present invention has been specifically disclosed by preferred embodiments and optional features, modification and variation of the inventions embodied therein herein disclosed may be resorted to by those skilled in the art, and that such modifications and variations are considered to be within the scope of this invention. The invention has been described broadly and generically herein. Each of the narrower species and subgeneric groupings falling within the generic disclosure also form part of the invention. This includes the generic description of the invention with a proviso or negative limitation removing any subject matter from the genus, regardless of whether or not the excised material is specifically recited herein. In addition, where features or aspects of the invention are described in terms of Markush groups, those skilled in the art will recognize that the invention is also thereby described in terms of any individual member or subgroup of members of the Markush group. Further embodiments of the invention will become apparent from the following claims.

CLAIMS

1. A compound according to Chemical Formula (I)

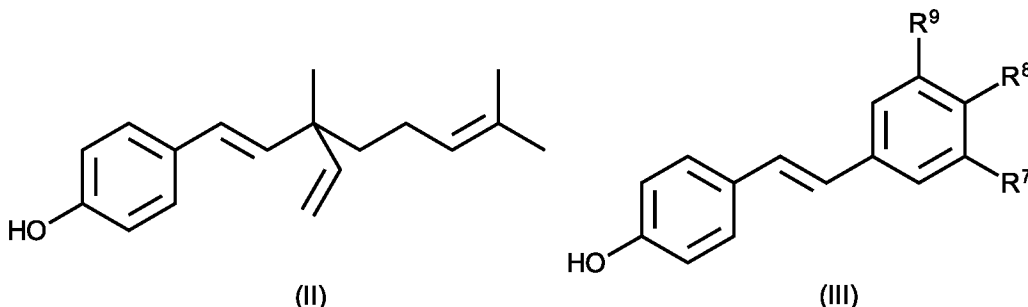


wherein, in Chemical Formula (I), R¹ is selected from the group consisting of C2-C15 (hetero)alkenyl, C2-C15 (hetero)alkynyl, C3-C15 (hetero)cycloalkyl, and (hetero)aryl, and R², R³, R⁴, R⁵ and R⁶ are each independently selected from the group consisting of halogen, H, OH, SH, and C1-C10 (hetero)alkyl, preferably from the group consisting of halogen, H, OH, SH, OCH₃, OCF₃, CH₂OH, COOH, COOCH₃, and O(CO)CH₃; or a pharmaceutically or cosmetically acceptable salt, prodrug, solvate, tautomer or stereoisomer thereof, for use in a method of decreasing lipid production in sebocytes.

2. The compound for use according to claim 1, wherein, in Chemical Formula (I), R¹ is selected from the group consisting of C2-C15 alkenyl, and aryl; and R², R³, R⁴, R⁵ and R⁶ are each independently selected from the group consisting of halogen, H, OH, SH, OCH₃, OCF₃, CH₂OH, COOH, COOCH₃, and O(CO)CH₃, preferably from the group consisting of H, OH, OCH₃, CH₂OH, COOH, COOCH₃, and O(CO)CH₃.
3. The compound for use according to claim 1 or claim 2, wherein R², R³, R⁴, R⁵ and R⁶ are not all H.
4. The compound for use according to any one of claims 1 to 3, wherein R⁴ is OH.
5. The compound for use according to any one of claims 1 to 4, wherein R⁴ is OH or SH; and R², R³, R⁵ and R⁶ are each independently H or F, preferably H.
6. The compound for use according to any one of claims 1 to 5, wherein R¹ is selected from the group consisting of C2-C10 alkenyl, and substituted phenyl, with substituents of the aforementioned groups being independently selected from the group consisting of halogen, OH, SH, OCH₃, OCF₃, COOH, COOCH₃, and COOCF₃, preferably from the group consisting of OH, SH, OCH₃, OCF₃, COOH, COOCH₃, and COOCF₃, more preferably from the group consisting of OH, OCH₃, COOH, and COOCH₃.

7. The compound for use according to claim 6, wherein R¹ is selected from the group consisting of substituted or unsubstituted, branched C₄-C₁₀ alkenyl, and substituted phenyl, with substituents of the aforementioned groups being independently selected from the group consisting of OH, SH, OCH₃, and OCF₃, preferably from the group consisting of OH and OCH₃.

8. The compound for use according to any one of claims 1 to 7, wherein the compound is a compound corresponding to Chemical Formula (II) or Chemical Formula (III)



wherein, in Chemical Formula (III), R⁷, R⁸ and R⁹ are each independently selected from the group consisting of H, F, OH, SH, OCH₃, and OCF₃, preferably from the group consisting of H, OH, and OCH₃.

9. The compound for use according to any one of claims 1 to 8, wherein the compound is selected from the group consisting of bakuchiol and pterostilbene.

10. The compound for use according to any one of claims 1 to 9, wherein the method is the treatment of a skin disease or disorder related to increased lipid production in sebocytes.

11. The compound for use according to claim 10, wherein the skin disease or disorder related to increased lipid production in sebocytes is selected from the group consisting of oily skin, shiny skin, skin having whiteheads and/or blackheads, skin having enlarged pores, and acne.

12. Composition comprising at least one compound as defined in any one of claims 1 to 9 and at least one cosmetically acceptable carrier.

13. The composition according to claim 12, wherein the composition is a

- topical composition; and/or
- cosmetic composition; and/or
- dermatological composition.

14. The composition according to claim 12 or claim 13, wherein the at least one compound as defined in any one of claims 1 to 8 is present in an amount of at least about 0.05 wt.-%, preferably in an amount of at least about 0.1 wt.-%, based on the total weight of the composition.

15. The composition according to claim any one of claims 12 to 14, wherein the at least one compound as defined in any one of claims 1 to 8 is present in an amount of about 0.05 to 50 wt.-%, preferably in an amount of about 0.1 to 40 wt.-%, more preferably in an amount of about 0.1 to 30 wt.-%, even more preferably in an amount of about 0.5 to 25 wt.-%, based on the total weight of the composition.
16. The composition according to any one of claims 12 to 15, wherein the composition further comprises at least one skin benefit agent.
17. The composition according to any one of claims 12 to 16, wherein the skin benefit agent is selected from the group consisting of moisturizing agents, antimicrobial agents, anti-inflammatory agents, antioxidants, UV absorbing agents, anti-acne agents, skin pigmentation-inducing agents, and skin pigmentation-blocking agents.
18. The composition according to any one of claims 12 to 17, wherein the composition further comprises at least one component selected from the group consisting of surfactants, solvents, sequestering agents, thickeners, fragrances, pH adjusters, preservatives, dyes, pigments, and opacifiers.
19. The composition according to any one of claims 12 to 18, wherein the composition is a skin cleanser, toner, serum, lotion, cream, emulsion, gel, make-up composition (foundation, make-up, powder), skin mask, hair mask, shampoo, or conditioner.
20. The composition according to any one of claims 12 to 19, wherein the composition is for decreasing lipid production in sebocytes.
21. Use of a composition according to any one of claims 12 to 20 for decreasing lipid production in sebocytes.
22. A cosmetic method for decreasing lipid production in sebocytes or in the skin of an individual in need thereof, comprising contacting said sebocyte or skin with lipid production-decreasing amount of at least one compound as defined in any one of claims 1 to 9 or composition according to any one of claims 12 to 20.

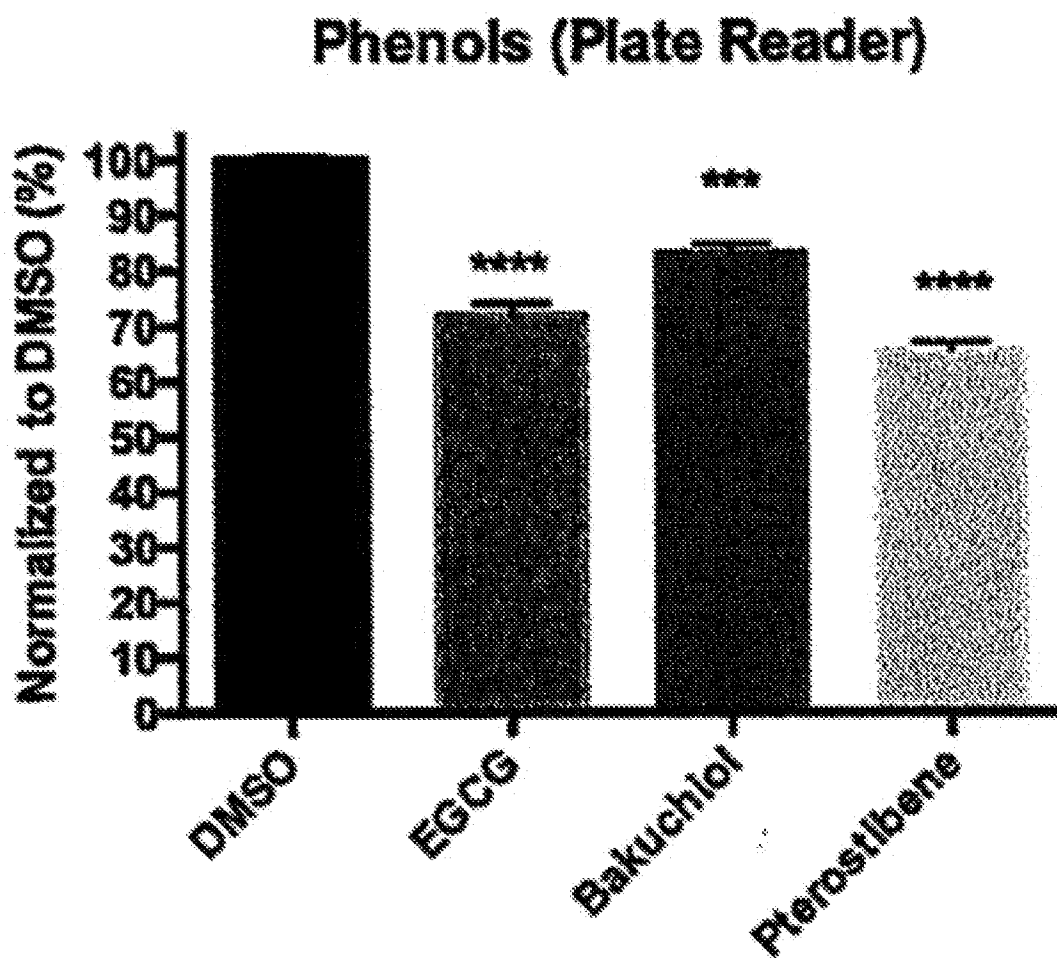


Figure 1

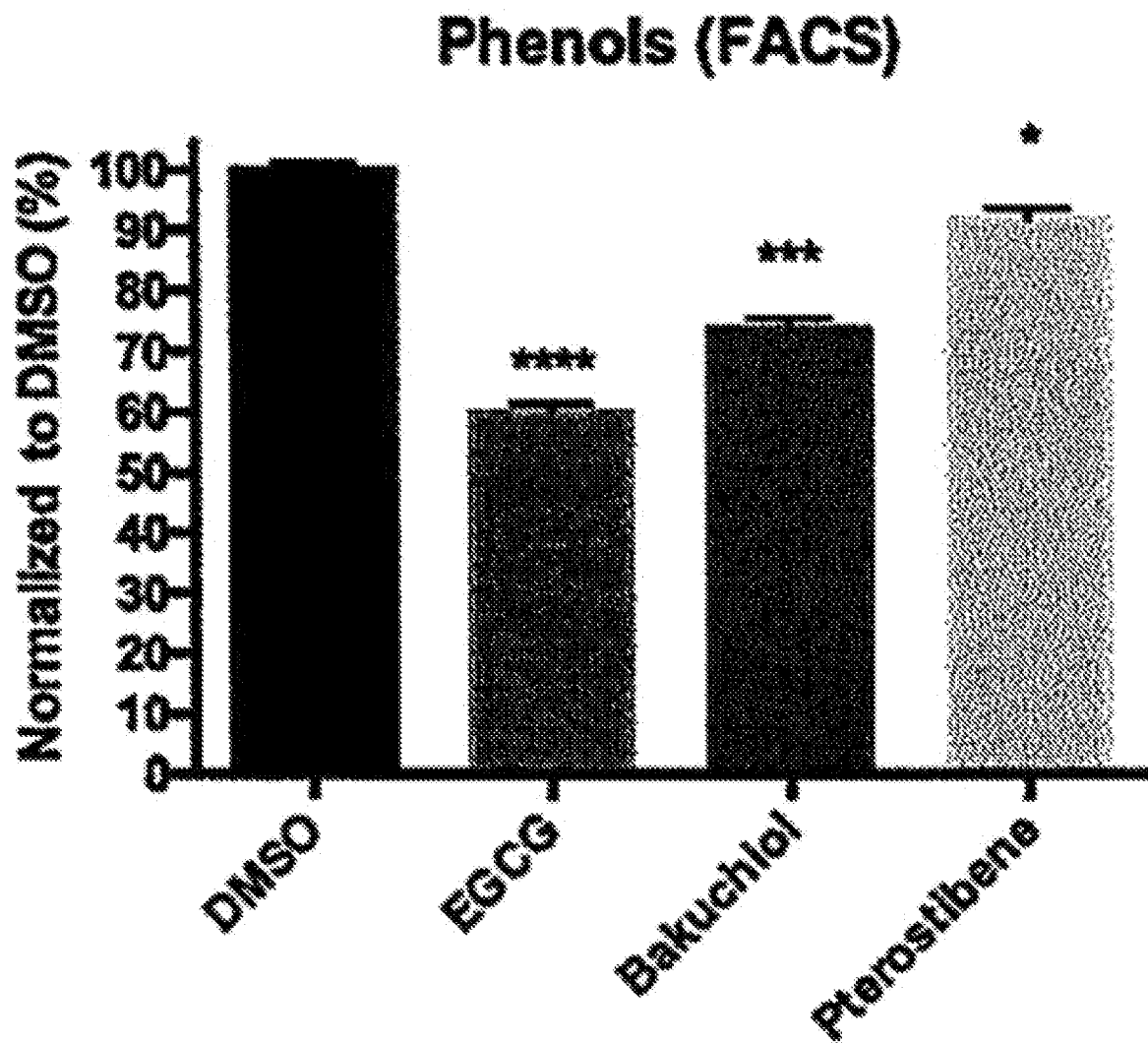


Figure 2

INTERNATIONAL SEARCH REPORT

International application No.

PCT/SG2020/050366

A. CLASSIFICATION OF SUBJECT MATTER

See Supplemental Box

According to International Patent Classification (IPC)

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CAS Registry, CAPlus, Medline, Biosis: Bakuchiol, Pterostilbene, Phenol, sebocytes, hyperseborrhoeic skin, seborrhoea, oily skin

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 2583662 A1 (THOREL J-N) 24 April 2013 ([0020]-[0027], [0034]-[0036], [0038]-[0044], [0079]-[0086] of the machine translation	1-22
X	WO 2014/134620 A1 (ENVY MEDICAL, INC.) 4 September 2014 para [05]-[08], [20], [17], [45]	1-22
X	CHAUDHURI, R. K. & MARCHIO, F., Bakuchiol in the management of acne-affected skin. Cosmetics & Toiletries magazine, Vol. 126, No. 7, pages 502-510. 16 July 2013 [Retrieved on 2020-09-30 from https://www.cosmeticsandtoiletries.com/formulating/function/antimicrobial/premium-Bakuchiol-in-the-Management-of-Acne-affected-Skin-215695021.html] Table 3, Fig 4, Pg 508 col 2, para 2	1-22

☒ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

*Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"D" document cited by the applicant in the international application

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

30/09/2020

(day/month/year)

Date of mailing of the international search report

05/10/2020

(day/month/year)

Name and mailing address of the ISA/SG

IP OS Intellectual Property Office of Singapore
1 Paya Lebar Link, #11-03
PLQ 1, Paya Lebar Quarter
Singapore 408533

Email: pct@ipos.gov.sg

Authorized officer

Toy Xiu Yi (Dr)

IPOS Customer Service Tel. No.: (+65) 6339 8616

INTERNATIONAL SEARCH REPORT

International application No.

PCT/SG2020/050366

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2011/051483 A1 (GREEN MOLECULAR, S.L.) 5 May 2011 Pg 4 line 5-10, Pg 6 line 29-Pg 10 line 9, Pg 11 line 6-15, Pg 19 line 11, Pg 20 line 4-6, Pg 36-38 Example 2	1-22
X	WO 01/43705 A2 (JOHNSON & JOHNSON CONSUMER COMPANIES, INC.) 21 June 2001 Pg 2 line 5-25, Pg 3 line 15-18, Pg 4 line 10-21, Pg 6 line 26-32, Pg 7 line 8-15, Pg 11 line 21-Pg 12 line 8, Examples	1-22
X	KIM, S. Y. ET AL., Resveratrol exerts growth inhibitory effects on human SZ95 sebocytes through the inactivation of the PI3-K/Akt pathway. <i>International Journal of Molecular Medicine</i> , 12 February 2015, Vol. 35, No. 4, pages 1042-1050 [Retrieved on 2020-09-30] <DOI: 10.3892/IJMM.2015.2098> Pg 1047, left col first para, Pg 1048, Figure 4, Pg 1049, left col line 46- right col line 3, Pg 1049 right col line 15-18	1-8, 12-13 and 20-22
X	WO 2004/034820 A2 (L'OREAL & NESTEC S.A.) 29 April 2004 Pg 7 line 25-Pg 8 line 25, Pg 9 line 11-20, Pg 10 line 8-15, Pg 11, line 7-14, Example 3	1-8, 10-18, 20-21

INTERNATIONAL SEARCH REPORT

International application No.

PCT/SG2020/050366

Supplemental Box (Classification of Subject Matter)

Int. Cl.

A61K 8/34 (2006.01)

A61K 31/05 (2006.01)

A61Q 19/00 (2006.01)

A61P 17/10 (2006.01)

A61P 17/08 (2006.01)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/SG2020/050366

Note: This Annex lists known patent family members relating to the patent documents cited in this International Search Report. This Authority is in no way liable for these particulars which are merely given for the purpose of information.

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 2583662 A1	24/04/2013	FR 2981275 A1 ES 2517516 T3	19/04/2013 03/11/2014
WO 2014/134620 A1	04/09/2014	US 2016/0206573 A1 US 2014/0249116 A1 ES 2744425 T3 BR 112015021124 A2 HK 1219877 A1 EP 2961418 A1 CN 105209051 A CA 2902977 A1	21/07/2016 04/09/2014 25/02/2020 18/07/2017 21/04/2017 06/01/2016 30/12/2015 04/09/2014
WO 2011/051483 A1	05/05/2011	RU 2012122241 A JP 2013509385 A AU 2016234952 A1 EP 2322159 A1 AU 2010311326 A1 ES 2432236 T3 MX 2012005013 A EP 2493462 A1 US 2016/0158164 A1 KR 20120094167 A CN 102639126 A CA 2778151 A1 US 2013/0136778 A1 BR 112012010070 A2 IL 219318 A US 2018/0008555 A1 DK 2493462 T3 JP 2016006060 A	10/12/2013 14/03/2013 13/10/2016 18/05/2011 17/05/2012 02/12/2013 15/08/2012 05/09/2012 09/06/2016 23/08/2012 15/08/2012 05/05/2011 30/05/2013 31/05/2016 31/03/2016 11/01/2018 28/10/2013 14/01/2016
WO 01/43705 A2	21/06/2001	AU 2094901 A	25/06/2001
WO 2004/034820 A2	29/04/2004	US 2006/0035846 A1 AU 2003293977 A1 EP 1553851 A2	16/02/2006 04/05/2004 20/07/2005