



US009498424B2

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

(10) **Patent No.:** **US 9,498,424 B2**

(45) **Date of Patent:** **Nov. 22, 2016**

(54) **ACTIVE MIXTURES OF ACYLATED OLIGOPEPTIDES AND TROXERUTIN**

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

(21) Appl. No.: **14/508,474**

(22) Filed: **Oct. 7, 2014**

(65) **Prior Publication Data**

US 2015/0105330 A1 Apr. 16, 2015

(30) **Foreign Application Priority Data**

Oct. 13, 2013 (EP) 13188402

(51) **Int. Cl.**

A61K 8/64 (2006.01)

A61K 38/08 (2006.01)

C07K 7/06 (2006.01)

A61Q 5/12 (2006.01)

A61Q 7/00 (2006.01)

A61K 8/60 (2006.01)

A61K 31/7048 (2006.01)

A61K 38/06 (2006.01)

(52) **U.S. Cl.**

CPC **A61K 8/64** (2013.01); **A61K 8/602** (2013.01); **A61K 31/7048** (2013.01); **A61K**

38/06 (2013.01); **A61K 38/08** (2013.01); **A61Q 5/12** (2013.01); **A61Q 7/00** (2013.01)

(58) **Field of Classification Search**

CPC **A61K 8/602**; **A61K 8/64**; **A61K 31/7048**; **A61K 38/08**; **A61K 38/06**; **A61K 2300/00**; **A61Q 7/00**; **A61Q 5/12**

See application file for complete search history.

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514/18.8

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(57) **ABSTRACT**

An active mixture having

(a) acylated oligopeptides, and

(b) troxerutin,

useful for increasing hair growth and in particular density of eyelashes and eyebrows.

17 Claims, No Drawings

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ACTIVE MIXTURES OF ACYLATED OLIGOPEPTIDES AND TROXERUTIN

FIELD OF INVENTION

The present invention refers to the area of cosmetics and relates to new active mixtures for increasing hair growth, in particular elongation and density of eyelashes and eyebrows.

STATE OF THE ART

Eyelash length, thickness and volume are key attributes for female customers that bring a glamorous expression to their eyes. In accordance to these needs nowadays mascaras should not only decorate the eyes, but should bring additional and long-term care benefits to eyelashes.

From the state of the art several actives are known for increasing hair growth in general and improve elongation and thickness of eyelashes in particular. For example, WO 2012 143845 A2 (Sederma) proposes for this purpose biotinoyl tripeptide-1, which is also known under the trademark "Widelash".

Another type of biosurfactant that is suggested for stimulation of the keratine gene expression is disclosed in WO 2007 143006 A2 (Therapeutic Peptides). The application deals with acylated oligopeptides of the general formula Acyl-AA-Term, in which Acyl stands for C₈-C₂₂ acyl radical, AA represents a sequence of 4 to 9 amino acids, and Term means an acid C-terminus or an amide C-terminus. However, in vivo test it was shown, that for increasing eye lash density and/or hair growth a minimum concentration of 50 to 100 ppm peptide/g serum is necessary. In other words: to achieve the desired effect relatively high concentrations of the peptides are necessary.

Therefore, the object underlying the present invention has been to provide an improved active or active mixture that simultaneously increases hair growth, in particular hair shaft elongation and density of eyelashes and eyebrows, at lower concentrations as reported in the state of the art, and is dermatological save.

DESCRIPTION OF THE INVENTION

Object of the present invention is an active mixture comprising

- (a) acylated oligopeptides and
- (b) troxerutin.

Surprisingly, it has been observed that the mixture leads to improved keratinocyte synthesis and thus fibre production, encourages the synthesis of adhesion molecules as for example laminin and collagen in the dermis/epithelium sheath junction, providing an optimal hair anchorage. For example using only 20 ppm of myristoyl pentapeptide-17 together with 0.1% troxerutin results in an increase in eyelash density of up to 15% in 28 days and of up to 22% in 42 days.

Acylated Oligopeptides

Acylated oligopeptides forming component (a) of the present invention are fully described in international patent application WO 200 143006 A2 (Therapeutic Peptides). As far as the structure and the manufacture of the components is concerned, this document is incorporated by reference. The oligopeptides show low critical micelle concentrations of typically less than about 100 ppm and can lower surface tension in an aqueous Minimal Essential Media (MEM) to less than about 50 dynes/cm². Preferably, component (a) is a C₆-C₂₂ acylated oligopeptide and/or an acylated oligopep-

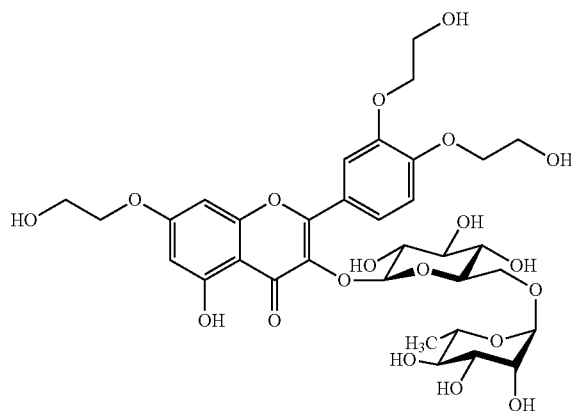
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ptide with 4 to 9 amino acid units, terminated either by an acid or an amide group or biotinoyl tripeptide-1. More preferably, component (a) is a C₆-C₂₂ acylated oligopeptide with 4 to 9 amino acid groups, terminated either with an acid or an amide group. The most preferred species is myristoyl pentapeptide-17.

Troxerutin

Troxerutin (component b) is a flavonol, a type of flavonoid. It is more accurately a hydroxy-ethylrutoside of formula (I):

Formula (I)



Troxerutin can be isolated from *Sophora japonica*, the Japanese pagoda tree and is mainly used as a vasoprotective (see C. Riccioni et al., *Minerva cardioangiologica* 52(1), p. 43-48 (2004)). Troxerutin has been shown in mice to reverse CNS insulin resistance and reduce reactive oxygen species induced by a high-cholesterol diet (see Lu et al., *Brain*, 134(3), p. 783-797 (2011)).

The acylated oligopeptides forming component (a) and troxerutin representing component (b) may be present in the mixture in a ratio by weight of from about 1:99 to about 99:1, preferably from about 25:75 to about 75:25 and more preferably from about 50:50 to about 90:10. The most preferred range is from about 80:20 to 98:2.

Cosmetic and/or Dermatological Compositions

Another object of the present invention is directed to a cosmetic and/or dermatological composition comprising the active mixture of component (a) and (b). Said composition may comprise the mixture in amounts of from about 0.01 to about 5% b.w, preferably from about 0.1 to about 2% b.w. and more preferably from about 0.5 to about 1% b.w. In another preferred embodiment, the composition is an eyelash conditioner.

The preparations according to the invention may also contain abrasives, anti-acne agents, agents against ageing of the skin, anti-cellulitis agents, antidandruff agents, anti-inflammatory agents, irritation-preventing agents, irritation-inhibiting agents, antioxidants, astringents, perspiration-inhibiting agents, antiseptic agents, anti-statics, binders, buffers, carrier materials, chelating agents, cell stimulants, cleansing agents, care agents, depilatory agents, surface-active substances, deodorizing agents, antiperspirants, softeners, emulsifiers, enzymes, essential oils, fibres, film-forming agents, fixatives, foam-forming agents, foam stabilizers, substances for preventing foaming, foam boosters, gelling agents, gel-forming agents, hair care agents, hair-setting agents, hair-straightening agents, moisture-donating agents,

moisturizing substances, moisture-retaining substances, bleaching agents, strengthening agents, stain-removing agents, optically brightening agents, impregnating agents, dirt-repellent agents, friction-reducing agents, lubricants, moisturizing creams, ointments, opacifying agents, plasticizing agents, covering agents, polish, gloss agents, polymers, powders, proteins, re-oiling agents, abrading agents, silicones, skin-soothing agents, skin-cleansing agents, skin care agents, skin-healing agents, skin-lightening agents, skin-protecting agents, skin-softening agents, hair promotion agents, cooling agents, skin-cooling agents, warming agents, skin-warming agents, stabilizers, UV-absorbing agents, UV filters, detergents, fabric conditioning agents, suspending agents, skin-tanning agents, thickeners, vitamins, oils, waxes, fats, phospholipids, saturated fatty acids, mono- or polyunsaturated fatty acids, α -hydroxy acids, polyhydroxyfatty acids, liquefiers, dyestuffs, colour-protecting agents, pigments, anti-corrosives, aromas, flavouring substances, odoriferous substances, polyols, surfactants, electrolytes, organic solvents or silicone derivatives and the like as additional auxiliaries and additives, peptide, oils (natural, mineral, vegetable).

A.1 Surfactants

Other preferred auxiliaries and additives are anionic and/or amphoteric or zwitterionic surfactants. Typical examples of anionic surfactants are soaps, alkyl benzenesulfonates, alkane-sulfonates, olefin sulfonates, alkylether sulfonates, glycerol ether sulfonates, methyl ester sulfonates, sulfofatty acids, alkyl sulfates, fatty alcohol ether sulfates, glycerol ether sulfates, fatty acid ether sulfates, hydroxy mixed ether sulfates, monoglyceride (ether) sulfates, fatty acid amide (ether) sulfates, mono- and dialkyl sulfosuccinates, mono- and dialkyl sulfosuccinamates, sulfotriglycerides, amide soaps, ether carboxylic acids and salts thereof, fatty acid isethionates, fatty acid sarcosinates, fatty acid taurides, N-acylamino acids such as, for example, acyl lactylates, acyl tartrates, acyl glutamates and acyl aspartates, alkyl oligoglucoside sulfates, alkyl polyglucoside sulfates, protein fatty acid condensates (particularly wheat-based vegetable products) and alkyl (ether) phosphates. If the anionic surfactants contain polyglycol ether chains, they may have a conventional homolog distribution although they preferably have a narrow-range homolog distribution. Typical examples of amphoteric or zwitterionic surfactants are alkylbetaines, alkylamidobetaines, aminopropionates, aminoglycinates, imidazolium betaines and sulfobetaines. The surfactants mentioned are all known compounds. Information on their structure and production can be found in relevant synoptic works, cf. for example J. Falbe (ed.), "*Surfactants in Consumer Products*", Springer Verlag, Berlin, 1987, pages 54 to 124 or J. Falbe (ed.), "*Katalysatoren, Tenside und Mineralöladditive (Catalysts, Surfactants and Mineral Oil Additives)*", Thieme Verlag, Stuttgart, 1978, pages 123-217. The percentage content of surfactants in the preparations may be from 0.1 to 10% by weight and is preferably from 0.5 to 5% by weight, based on the preparation.

A.2 Oil Bodies

Suitable oil bodies, which form constituents of the O/W emulsions, are, for example, Guerbet alcohols based on fatty alcohols having 6 to 18, preferably 8 to 10, carbon atoms, esters of linear C_6 - C_{22} -fatty acids with linear or branched C_6 - C_{22} -fatty alcohols or esters of branched C_6 - C_{13} -carboxylic acids with linear or branched C_6 - C_{22} -fatty alcohols, such as, for example, myristyl myristate, myristyl palmitate, myristyl stearate, myristyl isostearate, myristyl oleate, myristyl behenate, myristyl erucate, cetyl myristate, cetyl palmitate, cetyl stearate, cetyl isostearate, cetyl oleate, cetyl

behenate, cetyl erucate, stearyl myristate, stearyl palmitate, stearyl stearate, stearyl isostearate, stearyl oleate, stearyl behenate, stearyl erucate, isostearyl myristate, isostearyl palmitate, isostearyl stearate, isostearyl isostearate, isostearyl oleate, isostearyl behenate, isostearyl oleate, oleyl myristate, oleyl palmitate, oleyl stearate, oleyl isostearate, oleyl oleate, oleyl behenate, oleyl erucate, behenyl myristate, behenyl palmitate, behenyl stearate, behenyl isostearate, behenyl oleate, behenyl behenate, behenyl erucate, erucyl myristate, erucyl palmitate, erucyl stearate, erucyl isostearate, erucyl oleate, erucyl behenate and erucyl erucate. Also suitable are esters of linear C_6 - C_{22} -fatty acids with branched alcohols, in particular 2-ethylhexanol, esters of C_{18} - C_{38} -alkylhydroxy carboxylic acids with linear or branched C_6 - C_{22} -fatty alcohols, in particular Dioctyl Malate, esters of linear and/or branched fatty acids with polyhydric alcohols (such as, for example, propylene glycol, dimerdol or trimetriol) and/or Guerbet alcohols, triglycerides based on C_6 - C_{10} -fatty acids, liquid mono-/di-/triglyceride mixtures based on C_6 - C_{18} -fatty acids, esters of C_6 - C_{22} -fatty alcohols and/or Guerbet alcohols with aromatic carboxylic acids, in particular benzoic acid, esters of C_2 - C_{12} -dicarboxylic acids with linear or branched alcohols having 1 to 22 carbon atoms or polyols having 2 to 10 carbon atoms and 2 to 6 hydroxyl groups, vegetable oils, branched primary alcohols, substituted cyclohexanes, linear and branched C_6 - C_{22} -fatty alcohol carbonates, such as, for example, Dicaprylyl Carbonate (Cetiol® CC), Guerbet carbonates, based on fatty alcohols having 6 to 18, preferably 8 to 10, carbon atoms, esters of benzoic acid with linear and/or branched C_6 - C_{22} -alcohols (e.g. Finsolv® TN), linear or branched, symmetrical or asymmetrical dialkyl ethers having 6 to 22 carbon atoms per alkyl group, such as, for example, dicaprylyl ether (Cetiol® OE), ring-opening products of epoxidized fatty acid esters with polyols, silicone oils (cyclomethicones, silicone methicone grades, etc.) and/or aliphatic or naphthenic hydrocarbons, such as, for example, squalane, squalene or dialkylcyclohexanes.

A.3 Emulsifiers

Other surfactants may also be added to the preparations as emulsifiers, including for example:

products of the addition of 2 to 30 mol ethylene oxide and/or 0 to 5 mol propylene oxide onto linear C_{8-22} fatty alcohols, onto C_{12-22} fatty acids and onto alkyl phenols containing 8 to 15 carbon atoms in the alkyl group;

$C_{12/18}$ fatty acid monoesters and diesters of addition products of 1 to 30 mol ethylene oxide onto glycerol; glycerol mono- and diesters and sorbitan mono- and diesters of saturated and unsaturated fatty acids containing 6 to 22 carbon atoms and ethylene oxide addition products thereof;

addition products of 15 to 60 mol ethylene oxide onto castor oil and/or hydrogenated castor oil;

polyol esters and, in particular, polyglycerol esters such as, for example, polyglycerol polyricinoleate, polyglycerol poly-12-hydroxystearate or polyglycerol dimerate isostearate. Mixtures of compounds from several of these classes are also suitable;

addition products of 2 to 15 mol ethylene oxide onto castor oil and/or hydrogenated castor oil;

partial esters based on linear, branched, unsaturated or saturated $C_{6/22}$ fatty acids, ricinoleic acid and 12-hydroxystearic acid and glycerol, polyglycerol, pentaerythritol, -dipentaerythritol, sugar alcohols (for example sorbitol), alkyl glucosides (for example

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methyl glucoside, butyl glucoside, lauryl glucoside) and polyglucosides (for example cellulose); mono-, di and trialkyl phosphates and mono-, di- and/or tri-PEG-alkyl phosphates and salts thereof; wool wax alcohols; polysiloxane/polyalkyl polyether copolymers and corresponding derivatives; mixed esters of pentaerythritol, fatty acids, citric acid and fatty alcohol and/or mixed esters of C₆₋₂₂ fatty acids, methyl glucose and polyols, preferably glycerol or polyglycerol, polyalkylene glycols and glycerol carbonate.

The addition products of ethylene oxide and/or propylene oxide onto fatty alcohols, fatty acids, alkylphenols, glycerol mono- and diesters and sorbitan mono- and diesters of fatty acids or onto castor oil are known commercially available products. They are homologue mixtures of which the average degree of alkoxylation corresponds to the ratio between the quantities of ethylene oxide and/or propylene oxide and substrate with which the addition reaction is carried out. C_{12/18} fatty acid monoesters and diesters of addition products of ethylene oxide onto glycerol are known as lipid layer enhancers for cosmetic formulations. The preferred emulsifiers are described in more detail as follows:

(i) Partial glycerides. Typical examples of suitable partial glycerides are hydroxystearic acid monoglyceride, hydroxystearic acid diglyceride, isostearic acid monoglyceride, isostearic acid diglyceride, oleic acid monoglyceride, oleic acid diglyceride, ricinoleic acid monoglyceride, ricinoleic acid diglyceride, linoleic acid monoglyceride, linoleic acid diglyceride, linolenic acid monoglyceride, linolenic acid diglyceride, erucic acid monoglyceride, erucic acid diglyceride, tartaric acid monoglyceride, tartaric acid diglyceride, citric acid monoglyceride, citric acid diglyceride, malic acid monoglyceride, malic acid diglyceride and technical mixtures thereof which may still contain small quantities of triglyceride from the production process. Addition products of 1 to 30 and preferably 5 to 10 mol ethylene oxide onto the partial glycerides mentioned are also suitable.

(ii) Sorbitan esters. Suitable sorbitan esters are sorbitan monoisostearate, sorbitan sesquiisostearate, sorbitan diisostearate, sorbitan triisostearate, sorbitan monooleate, sorbitan sesquioleate, sorbitan dioleate, sorbitan trioleate, sorbitan monoerucate, sorbitan sesquierucate, sorbitan dierucate, sorbitan trierucate, sorbitan monoricinoleate, sorbitan sesquiricinoleate, sorbitan diricinoleate, sorbitan triricinoleate, sorbitan monohydroxystearate, sorbitan sesqui-hydroxystearate, sorbitan dihydroxystearate, sorbitan trihydroxystearate, sorbitan monotartrate, sorbitan sesquitartrate, sorbitan ditartrate, sorbitan tritartrate, sorbitan monocitrate, sorbitan sesquicitrate, sorbitan dicitrate, sorbitan tricitrate, sorbitan monomaleate, sorbitan sesquimaleate, sorbitan dimaleate, sorbitan trimaleate and technical mixtures thereof. Addition products of 1 to 30 and preferably 5 to 10 mol ethylene oxide onto the sorbitan esters mentioned are also suitable.

(iii) Polyglycerol esters. Typical examples of suitable polyglycerol esters are Polyglyceryl-2 Dipolyhydroxystearate (Dehymuls® PGPH), Polyglycerin-3-Diisostearate (Lameform® TGI), Polyglyceryl-4 Isostearate (Isolan® GI 34), Polyglyceryl-3 Oleate, Diisostearoyl Polyglyceryl-3 Diisostearate (Isolan® PDI), Polyglyceryl-3 Methylglucose Distearate (Tego Care® 450), Polyglyceryl-3 Beeswax (Cera Bellina®), Polyglyceryl-4 Caprate (Polyglycerol Caprate T2010/90), Polyglyceryl-3

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Cetyl Ether (Chimexane® NL), Polyglyceryl-3 Distearate (Cremophor® GS 32) and Polyglyceryl Polyricinoleate (Admul® WOL 1403), Polyglyceryl Dimerate Isostearate and mixtures thereof. Examples of other suitable polyolesters are the mono-, di- and triesters of trimethylol propane or pentaerythritol with lauric acid, cocofatty acid, tallow fatty acid, palmitic acid, stearic acid, oleic acid, behenic acid and the like optionally reacted with 1 to 30 mol ethylene oxide.

(iv) Anionic emulsifiers. Typical anionic emulsifiers are aliphatic C₁₂₋₂₂ fatty acids, such as palmitic acid, stearic acid or behenic acid for example, and C₁₂₋₂₂ dicarboxylic acids, such as azelaic acid or sebacic acid for example.

(v) Amphoteric emulsifiers. Other suitable emulsifiers are amphoteric or zwitterionic surfactants. Zwitterionic surfactants are surface-active compounds which contain at least one quaternary ammonium group and at least one carboxylate and one sulfonate group in the molecule. Particularly suitable zwitterionic surfactants are the so-called betaines, such as the N-alkyl-N,N-dimethyl ammonium glycinate, for example cocoalkyl dimethyl ammonium glycinate, N-acylaminopropyl-N,N-dimethyl ammonium glycinate, for example cocoacylaminopropyl dimethyl ammonium glycinate, and 2-alkyl-3-carboxymethyl-3-hydroxyethyl imidazolines containing 8 to 18 carbon atoms in the alkyl or acyl group and cocoacylaminooethyl hydroxyethyl carboxymethyl glycinate. The fatty acid amide derivative known under the CTFA name of Cocamidopropyl Betaine is particularly preferred. Ampholytic surfactants are also suitable emulsifiers. Ampholytic surfactants are surface-active compounds which, in addition to a C_{8/18} alkyl or acyl group, contain at least one free amino group and at least one —COOH— or —SO₃H— group in the molecule and which are capable of forming inner salts. Examples of suitable ampholytic surfactants are N-alkyl glycines, N-alkyl propionic acids, N-alkylaminobutyric acids, N-alkyliminodipropionic acids, N-hydroxyethyl-N-alkylamidopropyl glycines, N-alkyl taurines, N-alkyl sarcosines, 2-alkylaminopropionic acids and alkylaminooacetic acids containing around 8 to 18 carbon atoms in the alkyl group. Particularly preferred ampholytic surfactants are N-cocoalkylaminopropionate, cocoacylaminooethyl aminopropionate and C_{12/18} acyl sarcosine.

A.4 Superfatting Agents and Consistency Factors

Superfatting agents may be selected from such substances as, for example, lanolin and lecithin and also polyethoxylated or acylated lanolin and lecithin derivatives, polyol fatty acid esters, monoglycerides and fatty acid alkanolamides, the fatty acid alkanolamides also serving as foam stabilizers.

The consistency factors mainly used are fatty alcohols or hydroxyfatty alcohols containing 12 to 22 and preferably 16 to 18 carbon atoms and also partial glycerides, fatty acids or hydroxyfatty acids. A combination of these substances with alkyl oligoglucosides and/or fatty acid N-methyl glucamides of the same chain length and/or polyglycerol poly-12-hydroxystearates is preferably used.

A.5 Thickening Agents and Rheology Additives

Suitable thickeners are polymeric thickeners, such as Aerosil® types (hydrophilic silicas), polysaccharides, more especially xanthan gum, guar-guar, agar-agar, alginates and tyloses, carboxymethyl cellulose and hydroxyethyl cellulose, also relatively high molecular weight polyethylene glycol monoesters and diesters of fatty acids, polyacrylates (for example Carbopols® [Goodrich] or Synthalens® [Sigma]), polyacrylamides, polyvinyl alcohol and polyvinyl pyrrolidone, surfactants such as, for example, ethoxylated

fatty acid glycerides, esters of fatty acids with polyols, for example pentaerythritol or trimethylol propane, narrow-range fatty alcohol ethoxylates and electrolytes, such as sodium chloride and ammonium chloride.

A.6 Polymers

Suitable cationic polymers are, for example, cationic cellulose derivatives such as, for example, the quaternized hydroxyethyl cellulose obtainable from Amerchol under the name of Polymer JR 400®, cationic starch, copolymers of diallyl ammonium salts and acrylamides, quaternized vinyl pyrrolidone/vinyl imidazole polymers such as, for example, Luviquat® (BASF), condensation products of polyglycols and amines, quaternized collagen polypeptides such as, for example, Lauryldimonium Hydroxypropyl Hydrolyzed Collagen (Lamequat® L, Grünau), quaternized wheat polypeptides, polyethyleneimine, cationic silicone polymers such as, for example, amodimethicone, copolymers of adipic acid and dimethylaminohydroxypropyl diethylenetriamine (Cartaretine®, Sandoz), copolymers of acrylic acid with dimethyl diallyl ammonium chloride (Merquat® 550, Chemviron), polyaminopolyamides and crosslinked water-soluble polymers thereof, cationic chitin derivatives such as, for example, quaternized chitosan, optionally in microcrystalline distribution, condensation products of dihaloalkyls, for example dibromobutane, with bis-dialkylamines, for example bis-dimethylamino-1,3-propane, cationic guar gum such as, for example, Jaguar® CBS, Jaguar® C-17, Jaguar® C-16 of Celanese, quaternized ammonium salt polymers such as, for example, Mirapol® A-15, Mirapol® AD-1, Mirapol® AZ-1 of Miranol and the various polyquaternium types (for example 6, 7, 32 or 37) which can be found in the market under the tradenames Rheocare® CC or Ultragel® 300, native wheat protein, hydrolysed wheat protein (Dra-godermin), wheat bran extract.

Suitable anionic, zwitterionic, amphoteric and nonionic polymers are, for example, vinyl acetate/crotonic acid copolymers, vinyl pyrrolidone/vinyl acrylate copolymers, vinyl acetate/butyl maleate/isobornyl acrylate copolymers, methyl vinyl ether/maleic anhydride copolymers and esters thereof, uncrosslinked and polyol-crosslinked polyacrylic acids, acrylamidopropyl trimethylammonium chloride/acrylate copolymers, octylacrylamide/methyl methacrylate/tert.-butylaminoethyl methacrylate/2-hydroxypropyl methacrylate copolymers, polyvinyl pyrrolidone, vinyl pyrrolidone/vinyl acetate copolymers, vinyl pyrrolidone/dimethylaminoethyl methacrylate/vinyl caprolactam terpolymers and optionally derivatized cellulose ethers and silicones.

A.7 Pearlling Waxes

Suitable pearlling waxes are, for example, alkylene glycol esters, especially ethylene glycol distearate; fatty acid alkanolamides, especially cocofatty acid diethanolamide; partial glycerides, especially stearic acid monoglyceride; esters of polybasic, optionally hydroxy-substituted carboxylic acids with fatty alcohols containing 6 to 22 carbon atoms, especially long-chain esters of tartaric acid; fatty compounds, such as for example fatty alcohols, fatty ketones, fatty aldehydes, fatty ethers and fatty carbonates which contain in all at least 24 carbon atoms, especially laurone and distearyl ether; fatty acids, such as stearic acid, hydroxystearic acid or behenic acid, ring opening products of olefin epoxides containing 12 to 22 carbon atoms with fatty alcohols containing 12 to 22 carbon atoms and/or polyols containing 2 to 15 carbon atoms and 2 to 10 hydroxyl groups and mixtures thereof.

A.8 Silicones

Suitable silicone compounds are, for example, dimethyl polysiloxanes, methylphenyl polysiloxanes, cyclic silicones and amino-, fatty acid-, alcohol-, polyether-, epoxy-, fluo-rine-, glycoside- and/or alkyl-modified silicone compounds

which may be both liquid and resin-like at room temperature. Other suitable silicone compounds are simethicones which are mixtures of dimethicones with an average chain length of 200 to 300 dimethylsiloxane units and hydrogenated silicates. A detailed overview of suitable volatile silicones can be found in Todd et al. in *Cosm. Toil.* 91, 27 (1976).

A.9 Waxes and Stabilizers

Besides natural oils used, waxes may also be present in the preparations, more especially natural waxes such as, for example, candelilla wax, carnauba wax, Japan wax, espartograss wax, cork wax, guaruma wax, rice oil wax, sugar cane wax, ouricury wax, montan wax, beeswax, shellac wax, spermaceti, lanolin (wool wax), uropygial fat, ceresine, ozocerite (earth wax), petrolatum, paraffin waxes and micro-waxes; chemically modified waxes (hard waxes) such as, for example, montan ester waxes, sasol waxes, hydrogenated jojoba waxes and synthetic waxes such as, for example, polyalkylene waxes and polyethylene glycol waxes; shea butter vegetable oil, mineral oil.

Metal salts of fatty acids such as, for example, magnesium, aluminium and/or zinc stearate or ricinoleate may be used as stabilizers.

A.10 Primary Sun Protection Factors

Primary sun protection factors in the context of the invention are, for example, organic substances (light filters) which are liquid or crystalline at room temperature and which are capable of absorbing ultraviolet radiation and of releasing the energy absorbed in the form of longer-wave radiation, for example heat.

The formulations according to the invention advantageously contain at least one UV-A filter and/or at least one UV-B filter and/or a broadband filter and/or at least one inorganic pigment. Formulations according to the invention preferably contain at least one UV-B filter or a broadband filter, more particularly preferably at least one UV-A filter and at least one UV-B filter.

Preferred cosmetic compositions, preferably topical formulations according to the present invention comprise one, two, three or more sun protection factors selected from the group consisting of 4-aminobenzoic acid and derivatives, salicylic acid derivatives, benzophenone derivatives, dibenzoylmethane derivatives, diphenyl acrylates, 3-imidazol-4-yl acrylic acid and esters thereof, benzofuran derivatives, benzylidene malonate derivatives, polymeric UV absorbers containing one or more organosilicon radicals, cinnamic acid derivatives, camphor derivatives, trianilino-s-triazine derivatives, 2-hydroxyphenylbenzotriazole derivatives, phenylbenzimidazole sulfonic acid derivatives and salts thereof, anthranilic acid menthyl esters, benzotriazole derivatives and indole derivatives.

In addition, it is advantageous to combine compounds of formula (I) with active ingredients which penetrate into the skin and protect the skin cells from inside against sunlight-induced damage and reduce the level of cutaneous matrix metalloproteases. Preferred respective ingredients, so called arylhydrocarbon receptor antagonists, are described in WO 2007/128723, incorporated herein by reference. Preferred is 2-benzylidene-5,6-dimethoxy-3,3-dimethylindan-1-one.

The UV filters cited below which can be used within the context of the present invention are preferred but naturally are not limiting.

UV filters which are preferably used are selected from the group consisting of

- p-aminobenzoic acid
- p-aminobenzoic acid ethyl ester (25 mol) ethoxylated (INCI name: PEG-25 PABA)

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p-dimethylaminobenzoic acid-2-ethylhexyl ester
 p-aminobenzoic acid ethyl ester (2 mol)N-propoxylated
 p-aminobenzoic acid glycerol ester
 salicylic acid homomenthyl ester (homosalates) (Neo
 Heliopan®HMS)
 salicylic acid-2-ethylhexyl ester (Neo Heliopan®OS)
 triethanolamine salicylate
 4-isopropyl benzyl salicylate
 anthranilic acid menthyl ester (Neo Heliopan®MA)
 diisopropyl cinnamic acid ethyl ester
 p-methoxycinnamic acid-2-ethylhexyl ester (Neo
 Heliopan®AV)
 diisopropyl cinnamic acid methyl ester
 p-methoxycinnamic acid isoamyl ester (Neo Heliopan®E
 1000)
 p-methoxycinnamic acid diethanolamine salt
 p-methoxycinnamic acid isopropyl ester
 2-phenylbenzimidazole sulfonic acid and salts (Neo
 Heliopan®Hydro)
 3-(4'-trimethylammonium)benzylidene bornan-2-one
 methyl sulfate
 beta-imidazole-4(5)-acrylic acid (urocanic acid)
 3-(4'-sulfo)benzylidene bornan-2-one and salts
 3-(4'-methyl benzylidene)-D,L-camphor (Neo
 Heliopan®MBC)
 3-benzylidene-D,L-camphor
 N-[(2 and 4)-[2-(oxoborn-3-ylidene)methyl]benzyl]acry-
 lamide polymer
 4,4'-[(6-[4-(1,1-dimethyl)aminocarbonyl]phenylamino]-
 1,3,5-triazine-2,4-diyl)diimino]-bis-(benzoic acid-2-
 ethylhexyl ester) (Uvasorb®HEB)
 benzylidene malonate polysiloxane (Parsol®SLX)
 glyceryl ethylhexanoate dimethoxycinnamate
 dipropylene glycol salicylate
 tris(2-ethylhexyl)-4,4',4''-(1,3,5-triazine-2,4,6-triyltri-
 imino)tribenzoate (=2,4,6-trianilino-(p-carbo-2'-ethyl-
 hexyl-1'-oxy)-1,3,5-triazine) (Uvinul®T150)
 Broadband filters which are preferably combined with one
 or more compounds of formula (I) in a preparation accord-
 ing to the present invention are selected from the group
 consisting of
 2-ethylhexyl-2-cyano-3,3-diphenyl acrylate (Neo Helio-
 pan®303)
 ethyl-2-cyano-3,3'-diphenyl acrylate
 2-hydroxy-4-methoxybenzophenone (Neo
 Heliopan®BB)
 2-hydroxy-4-methoxybenzophenone-5-sulfonic acid
 dihydroxy-4-methoxybenzophenone
 2,4-dihydroxybenzophenone
 tetrahydroxybenzophenone
 2,2'-dihydroxy-4,4'-dimethoxybenzophenone
 2-hydroxy-4-n-octoxybenzophenone
 2-hydroxy-4-methoxy-4'-methyl benzophenone
 sodium hydroxymethoxybenzophenone sulfonate
 disodium-2,2'-dihydroxy-4,4'-dimethoxy-5,5'-disulfo-
 benzophenone
 phenol, 2-(2H-benzotriazol-2-yl)-4-methyl-6-(2-methyl-3
 (1,3,3,3-tetramethyl-1-(trimethylsilyl)oxy)disiloxa-
 nyl)propyl) (Mexoryl®XL)
 2,2'-methylene bis-(6-(2H-benzotriazol-2-yl)-4-1,1,3,3-
 tetramethylbutyl)phenol) (Tinosorb®M)
 2,4-bis-[4-(2-ethylhexyloxy)-2-hydroxyphenyl]-1,3,5-tri-
 azine
 2,4-bis-[[{4-(2-ethylhexyloxy)-2-hydroxy}phenyl]-6-(4-
 methoxyphenyl)-1,3,5-triazine (Tinosorb®S)

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2,4-bis-[[{4-(3-sulfonato)-2-hydroxypropyloxy)-2-
 hydroxy}phenyl]-6-(4-methoxyphenyl)-1,3,5-triazine
 sodium salt
 2,4-bis-[[{3-(2-propyloxy)-2-hydroxypropyloxy)-2-
 hydroxy}phenyl]-6-(4-methoxyphenyl)-1,3,5-triazine
 2,4-bis-[[{4-(2-ethylhexyloxy)-2-hydroxy}phenyl]-6-[4-
 (2-methoxyethyl carbonyl)phenylamino]-1,3,5-triazine
 2,4-bis-[[{4-(3-(2-propyloxy)-2-hydroxypropyloxy)-2-
 hydroxy}phenyl]-6-[4-(2-ethylcarboxyl)phe-
 nylamino]-1,3,5-triazine
 2,4-bis-[[{4-(2-ethylhexyloxy)-2-hydroxy}phenyl]-6-(1-
 methylpyrrol-2-yl)-1,3,5-triazine
 2,4-bis-[[{4-tris-(trimethylsiloxy)silylpropyloxy)-2-
 hydroxy}phenyl]-6-(4-methoxyphenyl)-1,3,5-triazine
 2,4-bis-[[{4-(2"-methylpropenyloxy)-2-hydroxy}phenyl]-
 6-(4-methoxyphenyl)-1,3,5-triazine
 2,4-bis-[[{4-(1',1',1',3',5',5',5'-hepta methylsiloxy-2"-
 methylpropyloxy)-2-hydroxy}phenyl]-6-(4-methoxy-
 phenyl)-1,3,5-triazine
 UV-A filters filters which are preferably combined with
 one or more compounds of formula (I) in a preparation
 according to the present invention are selected from the
 group consisting of
 4-isopropyl dibenzoyl methane
 terephthalylidene dibornane sulfonic acid and salts
 (Mexoryl®SX)
 4-t-butyl-4'-methoxydibenzoyl methane (avobenzene)/
 (Neo Heliopan®357)
 phenylene bis-benzimidazol tetrasulfonic acid disodium
 salt (Neo Heliopan®AP)
 2,2'-(1,4-phenylene)-bis-(1H-benzimidazole-4,6-disulfo-
 nic acid), monosodium salt
 2-(4-diethylamino-2-hydroxybenzoyl)benzoic acid hexyl
 ester (Uvinul® A Plus)
 indanylidene compounds in accordance with DE 100 55
 940 A1 (=WO 2002 038537 A1)
 UV filters which are more preferably combined with one
 or more compounds of formula (I) in a preparation accord-
 ing to the present invention are selected from the group
 consisting of
 p-aminobenzoic acid
 3-(4'-trimethylammonium)benzylidene bornan-2-one
 methyl sulfate
 salicylic acid homomenthyl ester (Neo Heliopan®HMS)
 2-hydroxy-4-methoxybenzophenone (Neo
 Heliopan®BB)
 2-phenylbenzimidazole sulfonic acid (Neo
 Heliopan®Hydro)
 terephthalylidene dibornane sulfonic acid and salts
 (Mexoryl®SX)
 4-tert-butyl-4'-methoxydibenzoyl methane (Neo Helio-
 pan®357)
 3-(4'-sulfo)benzylidene bornan-2-one and salts
 2-ethylhexyl-2-cyano-3,3-diphenyl acrylate (Neo Helio-
 pan®303)
 N-[(2 and 4)-[2-(oxoborn-3-ylidene)methyl]benzyl]acry-
 lamide polymer
 p-methoxycinnamic acid-2-ethylhexyl ester (Neo
 Heliopan®AV)
 p-aminobenzoic acid ethyl ester (25 mol) ethoxylated
 (INCI name: PEG-25 PABA)
 p-methoxycinnamic acid isoamyl ester (Neo
 Heliopan®E1000)
 2,4,6-trianilino-(p-carbo-2'-ethylhexyl-1'-oxy)-1,3,5-tri-
 azine (Uvinul®T150)

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phenol, 2-(2H-benzotriazol-2-yl)-4-methyl-6-(2-methyl-3-(1,3,3,3-tetramethyl-1-(trimethylsilyloxy)disiloxanyl)propyl) (Mexoryl®XL)
 4,4'-[(6-[4-(1,1-dimethyl)aminocarbonyl]phenylamino)-1,3,5-triazine-2,4-diyl]diimino]-bis-(benzoic acid-2-ethylhexyl ester) (Uvasorb HEB)
 3-(4'-methyl benzylidene)-D,L-camphor (Neo Heliopan®MBC)
 3-benzylidene camphor
 salicylic acid-2-ethylhexyl ester (Neo Heliopan®OS)
 4-dimethylaminobenzoic acid-2-ethylhexyl ester (Padimate O)
 hydroxy-4-methoxybenzophenone-5-sulfonic acid and Na salt
 2,2'-methylene bis-(6-(2H-benzotriazol-2-yl)-4-1,1,3,3-tetramethyl butyl) phenol (Tinosorb®M)
 phenylene bis-benzimidazol tetrasulfonic acid disodium salt (Neo Heliopan®AP)
 2,4-bis-[(4-(2-ethylhexyloxy)-2-hydroxy}phenyl]-6-(4-methoxyphenyl)-1,3,5-triazine (Tinosorb®S)
 benzylidene malonate polysiloxane (Parsol®SLX)
 menthyl anthranilate (Neo Heliopan®MA)
 2-(4-diethylamino-2-hydroxybenzoyl)benzoic acid hexyl ester (Uvinul® A Plus)
 indanylidene compounds in accordance with DE 100 55 940 (=WO 02/38537).

Advantageous primary and also secondary sun protection factors are mentioned in WO 2005 123101 A1. Advantageously, these preparations contain at least one UVA filter and/or at least one UVB filter and/or at least one inorganic pigment. The preparations may be present here in various forms such as are conventionally used for sun protection preparations. Thus, they may be in form of a solution, an emulsion of the water-in-oil type (W/O) or of the oil-in-water type (O/W) or a multiple emulsion, for example of the water-in-oil-in-water type (W/O/W), a gel, a hydrodispersion, a solid stick or else an aerosol.

In a further preferred embodiment a formulation according to the invention contains a total amount of sunscreen agents, i.e. in particular UV filters and/or inorganic pigments (UV filtering pigments) so that the formulation according to the invention has a light protection factor of greater than or equal to 2 (preferably greater than or equal to 5). Such formulations according to the invention are particularly suitable for protecting the skin and hair.

A.11 Secondary Sun Protection Factors

Besides the groups of primary sun protection factors mentioned above, secondary sun protection factors of the antioxidant type may also be used. Secondary sun protection factors of the antioxidant type interrupt the photochemical reaction chain which is initiated when UV rays penetrate into the skin. Typical examples are amino acids (for example *glycine*, histidine, tyrosine, tryptophane) and derivatives thereof, imidazoles (for example urocanic acid) and derivatives thereof, peptides, such as D,L-carnosine, D-carnosine, L-carnosine and derivatives thereof (for example anserine), carotinoids, carotenes (for example alpha-carotene, beta-carotene, lycopene) and derivatives thereof, chlorogenic acid and derivatives thereof, liponic acid and derivatives thereof (for example dihydroliponic acid), aurothioglucose, propylthiouracil and other thiols (for example thioredoxine, glutathione, cysteine, cystine, cystamine and glycosyl, N-acetyl, methyl, ethyl, propyl, amyl, butyl and lauryl, palmitoyl, oleyl, alpha-linoleyl, cholesteryl and glyceryl esters thereof) and their salts, dilaurylthiodipropionate, distearylthiodipropionate, thiodipropionic acid and derivatives thereof (esters, ethers, peptides, lipids, nucleotides, nucleo-

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sides and salts) and sulfoximine compounds (for example butionine sulfoximines, homocysteine sulfoximine, butionine sulfones, penta-, hexa- and hepta-thionine sulfoximine) in very small compatible dosages, also (metal) chelators (for example alpha-hydroxyfatty acids, palmitic acid, phytic acid, lactoferrine), alpha-hydroxy acids (for example citric acid, lactic acid, malic acid), humic acid, bile acid, bile extracts, bilirubin, biliverdin, EDTA, EGTA and derivatives thereof, unsaturated fatty acids and derivatives thereof (for example linoleic acid, oleic acid), folic acid and derivatives thereof, ubiquinone and ubiquinol and derivatives thereof, vitamin C and derivatives thereof (for example ascorbyl palmitate, Mg ascorbyl phosphate, ascorbyl acetate), tocopherols and derivatives (for example vitamin E acetate), vitamin A and derivatives (vitamin A palmitate) and conferyl benzoate of benzoin resin, rutinic acid and derivatives thereof, glycosyl rutin, ferulic acid, furfurylidene glucitol, carnosine, butyl hydroxytoluene, butyl hydroxyanisole, nordihydroguaiaic resin acid, nordihydroguaiaietic acid, trihydroxybutyrophenone, uric acid and derivatives thereof, mannose and derivatives thereof, superoxide dismutase, titanium dioxide (for example dispersions in ethanol), zinc and derivatives thereof (for example ZnO, ZnSO₄), selenium and derivatives thereof (for example selenium methionine), stilbenes and derivatives thereof (for example stilbene oxide, trans-stilbene oxide) and derivatives of these active substances suitable for the purposes of the invention (salts, esters, ethers, sugars, nucleotides, nucleosides, peptides and lipids).

Advantageous inorganic secondary light protection pigments are finely dispersed metal oxides and metal salts which are also mentioned in WO 2005 123101 A1. The total quantity of inorganic pigments, in particular hydrophobic inorganic micro-pigments in the finished cosmetic preparation according to the present invention is advantageously from 0.1 to 30% by weight, preferably 0.5 to 10.0% by weight, in each case based on the total weight of the preparation.

Also preferred are particulate UV filters or inorganic pigments, which can optionally be hydrophobed, can be used, such as the oxides of titanium (TiO₂), zinc (ZnO), iron (Fe₂O₃), zirconium (ZrO₂), silicon (SiO₂), manganese (e.g. MnO), aluminium (Al₂O₃), cerium (e.g. Ce₂O₃) and/or mixtures thereof.

A.12 Active Modulating Skin and/or Hair Pigmentation

Preferred active ingredients for skin and/or hair lightening are selected from the group consisting of:

kojic acid (5-hydroxy-2-hydroxymethyl-4-pyranone), kojic acid derivatives, preferably kojic acid dipalmitate, arbutin, ascorbic acid, ascorbic acid derivatives, preferably magnesium ascorbyl phosphate, hydroquinone, hydroquinone derivatives, resorcinol, resorcinol derivatives, preferably 4-alkylresorcinols and 4-(1-phenylethyl)1,3-dihydroxybenzene (phenylethyl resorcinol), cyclohexylcarbamates (preferably one or more cyclohexyl carbamates disclosed in WO 2010/122178 and WO 2010/097480), sulfur-containing molecules, preferably glutathione or cysteine, alpha-hydroxy acids (preferably citric acid, lactic acid, malic acid), salts and esters thereof, N-acetyl tyrosine and derivatives, undecenoyl phenylalanine, gluconic acid, chromone derivatives, preferably aloesin, flavonoids, 1-aminoethyl phosphinic acid, thiourea derivatives, ellagic acid, nicotinamide (niacinamide), zinc salts, preferably zinc chloride or zinc gluconate, thujaplicin and derivatives, triterpenes, preferably maslinic acid, sterols, preferably ergosterol, benzofuranones, preferably senkyunolide, vinyl guaiacol, ethyl guaiacol, dionic acids, preferably octadecene dionic acid and/or aze-

laic acid, inhibitors of nitrogen oxide synthesis, preferably L-nitroarginine and derivatives thereof, 2,7-dinitroindazole or thiocitrulline, metal chelators (preferably alpha-hydroxy fatty acids, phytic acid, humic acid, bile acid, bile extracts, EDTA, EGTA and derivatives thereof), retinoids, soy milk and extract, serine protease inhibitors or lipoic acid or other synthetic or natural active ingredients for skin and hair lightening, the latter preferably used in the form of an extract from plants, preferably bearberry extract, rice extract, *papaya* extract, turmeric extract, mulberry extract, bengkoang extract, nutgrass extract, liquorice root extract or constituents concentrated or isolated therefrom, preferably glabridin or licochalcone A, *artocarpus* extract, extract of *rumex* and ramulus species, extracts of pine species (*pinus*), extracts of *vitis* species or stilbene derivatives isolated or concentrated therefrom, saxifrage extract, scutellaria extract, grape extract and/or microalgae extract, in particular *Tetraselmis suecica* Extract, *Isochrysis galbana* extract.

Preferred skin lighteners as component (b) are kojic acid and phenylethyl resorcinol as tyrosinase inhibitors, beta- and alpha-arbutin, hydroquinone, nicotinamide, dioic acid, Mg ascorbyl phosphate and vitamin C and its derivatives, mulberry extract, Bengkoang extract, *papaya* extract, turmeric extract, nutgrass extract, licorice extract (containing glycyrrhizin), alpha-hydroxy-acids, 4-alkylresorcinols, 4-hydroxy-anisole. These skin lighteners are preferred due to their very good activity, in particular in combination with sclareolide according to the present invention. In addition, said preferred skin lighteners are readily available.

Advantageous skin and hair tanning active ingredients in this respect are substrates or substrate analogues of tyrosinase such as L-tyrosine, N-acetyl tyrosine, L-DOPA or L-dihydroxyphenylalanine, xanthine alkaloids such as caffeine, theobromine and theophylline and derivatives thereof, proopiomelanocortin peptides such as ACTH, alpha-MSH, peptide analogues thereof and other substances which bind to the melanocortin receptor, peptides such as Val-Gly-Val-Ala-Pro-Gly, Lys-Ile-Gly-Arg-Lys or Leu-Ile-Gly-Lys, purines, pyrimidines, folic acid, copper salts such as copper gluconate, chloride or pyrrolidonate, 1,3,4-oxadiazole-2-thiols such as 5-pyrazin-2-yl-1,3,4-oxadiazole-2-thiol, curcumin, zinc diglycinate (Zn(Gly)₂), manganese(II) bicarbonate complexes ("pseudocat-alases") as described for example in EP 0 584 178, tetrasubstituted cyclohexene derivatives as described for example in WO 2005/032501, isoprenoids as described in WO 2005/102252 and in WO 2006/010661, melanin derivatives such as Melasyn-100 and MelanZe, diacyl glycerols, aliphatic or cyclic diols, psoralens, prostaglandins and analogues thereof, activators of adenylate cyclase and compounds which activate the transfer of melanosomes to keratinocytes such as serine proteases or agonists of the PAR-2 receptor, extracts of plants and plant parts of the *chrysanthemum* species, san-guisorba species, walnut extracts, urucum extracts, rhubarb extracts, microalgae extracts, in particular *Isochrysis galbana*, trehalose, erythrose and dihydroxyacetone. Flavonoids which bring about skin and hair tinting or brown-ing (e.g. quercetin, rhamnetin, kaempferol, fisetin, genistein, daidzein, chrysin and api-genin, epicatechin, diosmin and diosmetin, morin, quercitrin, naringenin, hesperidin, phloridzin and phloretin) can also be used.

The amount of the aforementioned examples of additional active ingredients for the modulation of skin and hair pigmentation (one or more compounds) in the products according to the invention is then preferably 0.00001 to 30

wt. %, preferably 0.0001 to 20 wt. %, particularly preferably 0.001 to 5 wt. %, based on the total weight of the preparation.

A.13 Anti-Ageing Actives

In the context of the invention, anti-ageing or biogenic agents are, for example antioxidants, matrix-metalloproteinase inhibitors (MMPI), skin moisturizing agents, glycosaminoglycan stimulators, anti-inflammatory agents, TRPV1 antagonists and plant extracts, stem cell protectors.

- (i) Antioxidants. Suitable antioxidants encompass amino acids (preferably *glycine*, histidine, tyrosine, tryptophan) and derivatives thereof, imidazoles (preferably urocanic acid) and derivatives thereof, peptides, preferably D,L-carnosine, D-carnosine, L-carnosine and derivatives thereof (preferably anserine), carnitine, creatine, matrikine peptides (preferably lysyl-threonyl-threonyl-lysyl-serine) and palmitoylated pentapeptides, carotenoids, carotenes (preferably alpha-carotene, beta-carotene, lycopene) and derivatives thereof, lipoic acid and derivatives thereof (preferably dihydrolipoic acid), aurothiogluucose, propyl thiouracil and other thiols (preferably thioredoxine, glutathione, cysteine, cystine, cystamine and glycosyl, N-acetyl, methyl, ethyl, propyl, amyl, butyl and lauryl, palmitoyl, oleyl, gamma-linoleyl, cholesteryl, glyceryl and oligoglycerol esters thereof) and salts thereof, dilauryl thiodipropionate, distearyl thiodipropionate, thiodipropionic acid and derivatives thereof (preferably esters, ethers, peptides, lipids, nucleotides, nucleosides and salts) and sulfoximine compounds (preferably buthionine sulfoximines, homocysteine sulfoximine, buthionine sulfones, penta-, hexa-, heptathionine sulfoximine) in very small tolerated doses (e.g. pmol to μmol/kg), also (metal) chelators (preferably alpha-hydroxy fatty acids, palmitic acid, phytic acid, lactoferrin, alpha-hydroxy acids (preferably citric acid, lactic acid, malic acid), humic acid, bile acid, bile extracts, tannins, bilirubin, biliverdin, EDTA, EGTA and derivatives thereof), unsaturated fatty acids and derivatives thereof (preferably gamma-linolenic acid, linoleic acid, oleic acid), folic acid and derivatives thereof, ubiquinone and derivatives thereof, ubiquinol and derivatives thereof, vitamin C and derivatives (preferably ascorbyl palmitate, Mg ascorbyl phosphate, ascorbyl acetate, ascorbyl glucoside), tocopherols and derivatives (preferably vitamin E acetate), vitamin A and derivatives (vitamin A palmitate) and coniferyl benzoate of benzoic resin, rutinic acid and derivatives thereof, flavonoids and glycosylated precursors thereof, in particular quercetin and derivatives thereof, preferably alpha-glucosyl rutin, rosmarinic acid, carnosol, carnosolic acid, resveratrol, caffeic acid and derivatives thereof, sinapic acid and derivatives thereof, ferulic acid and derivatives thereof, curcuminoids, chlorogenic acid and derivatives thereof, retinoids, preferably retinyl palmitate, retinol or tretinoin, ursolic acid, levulinic acid, butyl hydroxytoluene, butyl hydroxyanisole, nordihydroguaiac acid, nordihydroguaiaretic acid, trihydroxybutyrophene, uric acid and derivatives thereof, mannose and derivatives thereof, zinc and derivatives thereof (preferably ZnO, ZnSO₄), selenium and derivatives thereof (preferably selenium methionine), superoxide dismutase, stilbenes and derivatives thereof (preferably stilbene oxide, trans-stilbene oxide) and the derivatives (salts, esters, ethers, sugars, nucleotides, nucleosides, peptides and lipids) of these cited active ingredients which are suitable according to the invention or extracts or fractions of plants having an antioxidant effect, preferably green tea, rooibos, honeybush, grape, rosemary, sage, *melissa*,

thyme, lavender, olive, oats, cocoa, ginkgo, *ginseng*, liquorice, honeysuckle, *sophora*, *pueraria*, *pinus*, citrus, *Phyllanthus emblica* or St. John's wort, grape seeds, wheat germ, *Phyllanthus emblica*, coenzymes, preferably coenzyme Q10, plastoquinone and menaquinone. Preferred antioxidants are selected from the group consisting of vitamin A and derivatives, vitamin C and derivatives, tocopherol and derivatives, preferably tocopheryl acetate, and ubiquinone; *Purpurea Echinacea* extract or powder, terpenes, (especially bisabolol, ginger extract or 6-paradol, glycyrrhizic acid or derivatives glycyrrhetic acid or derivatives.

If vitamin E and/or derivatives thereof are used as the antioxidant(s), it is advantageous to choose their concentrations from the range from about 0.001 to about 10% b.w. based on the total weight of the formulation. If vitamin A or vitamin A derivatives or carotenes or derivatives thereof are used as the antioxidant(s), it is advantageous to choose their concentrations from the range from about 0.001 to about 10% b.w. based on the total weight of the formulation.

(ii) Matrix-Metalloproteinase inhibitors (MMPI). Preferred compositions comprise matrix-metalloproteinase inhibitors, especially those inhibiting matrix-metalloproteinases enzymatically cleaving collagen, selected from the group consisting of: ursolic acid, retinyl palmitate, propyl galate, precocenes, 6-hydroxy-7-methoxy-2,2-dimethyl-1 (2H)-benzopyran, 3,4-dihydro-6-hydroxy-7-methoxy-2, 2-dimethyl-1 (2H)-benzopyran, benzamidine hydrochloride, the cysteine proteinase inhibitors N-ethylmaleimide and epsilon-amino-n-caproic acid of the serine-protease inhibitors: phenylmethylsulfonyl-fluoride, collibinin (company Pentapharm; INCI: hydrolysed rice protein), oenotherol (company Soliance; INCI: propylene glycol, aqua, *Oenothera biennis* root extract, ellagic acid and ellagitannins, for example from pomegranate), phosphoramidone hinokitiol, EDTA, galardin, EquiStat (company Collaborative Group; apple fruit extract, soya seed extract, ursolic acid, soya isoflavones and soya proteins), sage extracts, MDI (company Atrium; INCI: glycosaminoglycans), fermiskin (company Silab/Mawi; INCI: water and lentinus *edodes* extract), actimp 1.9.3 (company Expanscience/Rahn; INCI: hydrolysed lupine protein), lipobelle soyaglycone (company Mibelle; INCI: alcohol, polysorbate 80, lecithin and soy isoflavones), extracts from green and black tea and further plant extracts, which are listed in WO 02 069992 A1 (see tables 1-12 there, incorporated herein by reference), proteins or glycoproteins from soya, hydrolysed proteins from rice, pea or lupine, plant extracts which inhibit MMPs, preferably extracts from shitake mushrooms, extracts from the leaves of the Rosaceae family, sub-family Rosoideae, quite particularly extracts of blackberry leaf (preferably as described in WO 2005 123101 A1, incorporated herein by reference) as e.g. SymMatrix (company Symrise, INCI: Maltodextrin, *Rubus Fruticosus* (Blackberry) Leaf Extract). Preferred actives of are selected from the group consisting of retinyl palmitate, ursolic acid, extracts from the leaves of the Rosaceae family, sub-family Rosoideae, genistein and daidzein.

(iii) Skin-moisturizing agents. Preferred skin moisturizing agents are selected from the group consisting of alkane diols or alkane triols comprising 3 to 12 carbon atoms, preferably C₃-C₁₀-alkane diols and C₃-C₁₀-alkane triols. More preferably the skin moisturizing agents are selected from the group consisting of: glycerol, 1,2-propylene glycol, 1,2-butylene glycol, 1,3-butylene glycol, 1,2-pen-

tanediol, 1,2-hexanediol, 1,2-octanediol and 1,2-decanediol, sugars (e.g. trehalose and glucose).

(iv) Glycosaminoglycan stimulators. Preferred compositions comprise substances stimulating the synthesis of glycosaminoglycans selected from the group consisting of hyaluronic acid and derivatives or salts, Subliskin (Sederma, INCI: *Sinorhizobium Meliloti* Ferment Filtrate, Cetyl Hydroxyethylcellulose, Lecithin), Hyalufix (BASF, INCI: Water, Butylene Glycol, *Alpinia galanga* leaf extract, Xanthan Gum, Caprylic/Capric Triglyceride), Stimulhyal (Soliance, INCI: Calcium ketogluconate), Syn-Glycan (DSM, INCI: Tetradecyl Aminobutyroylvalylaminobutyric Urea Trifluoroacetate, Glycerin, Magnesium chloride), Kalpariane (Biotech Marine), DC Upregulex (Distinctive Cosmetic Ingredients, INCI: Water, Butylene Glycol, Phospholipids, Hydrolyzed Sericin), glucosamine, N-acetyl glucosamine, retinoids, preferably retinol and vitamin A, *Arctium lappa* fruit extract, *Eriobotrya japonica* extract, Genkwanin, N-Methyl-L-serine, (-)-alpha-bisabolol or synthetic alpha-bisabolol such as e.g. Dragosantol and Dragosantol 100 from Symrise, oat glucan, *Echinacea purpurea* extract and soy protein hydrolysate. Preferred actives are selected from the group consisting of hyaluronic acid and derivatives or salts, retinol and derivatives, (-)-alpha-bisabolol or synthetic alpha-bisabolol such as e.g. Dragosantol and Dragosantol 100 from Symrise, oat glucan, *Echinacea purpurea* extract, *Sinorhizobium Meliloti* Ferment Filtrate, Calcium ketogluconate, *Alpinia galanga* leaf extract and tetradecyl aminobutyroylvalylaminobutyric urea trifluoroacetate.

(v) Anti-inflammatory agents. The compositions may also contain anti-inflammatory and/or redness and/or itch ameliorating ingredients, in particular steroidal substances of the corticosteroid type selected from the group consisting of hydrocortisone, dexamethasone, dexamethasone phosphate, methyl prednisolone or cortisone, are advantageously used as anti-inflammatory active ingredients or active ingredients to relieve reddening and itching, the list of which can be extended by the addition of other steroidal anti-inflammatories. Non-steroidal anti-inflammatories can also be used. Examples which can be cited here are oxicams such as piroxicam or tenoxicam; salicylates such as aspirin, disalcid, solprin or fendosal; acetic acid derivatives such as diclofenac, fenclofenac, indomethacin, sulindac, tolmetin or clindanac; fenamates such as mefenamic, meclofenamic, flufenamic or niflumic; propionic acid derivatives such as ibuprofen, naproxen, benoxaprofen or pyrazoles such as phenylbutazone, oxyphenylbutazone, febrazole or azapropazone. Anthranilic acid derivatives, in particular avenanthramides described in WO 2004 047833 A1, are preferred anti-itch ingredients in a composition according to the present invention.

Also useful are natural or naturally occurring anti-inflammatory mixtures of substances or mixtures of substances that alleviate reddening and/or itching, in particular extracts or fractions from camomile, Aloe vera, *Commiphora* species, *Rubia* species, willow, willowherb, oats, *calendula*, *arnica*, St John's wort, honeysuckle, rosemary, *Passiflora incarnata*, witch hazel, ginger or *Echinacea*; preferably selected from the group consisting of extracts or fractions from camomile, Aloe vera, oats, *calendula*, *arnica*, honeysuckle, rosemary, witch hazel, ginger or *Echinacea*, and/or pure substances, preferably alpha-bisabolol, apigenin, apigenin-7-glucoside, gingerols, shogaols, gingerdiols, dehydrogingerdiones, paradols, natural or naturally occurring avenanthramides, preferably tranilast,

avenanthramide A, avenanthramide B, avenanthramide C, non-natural or non-naturally occurring avenanthramides, preferably dihydroavenanthramide D, dihydroavenanthramide E, avenanthramide D, avenanthramide E, avenanthramide F, boswellic acid, 5
phytosterols, glycyrrhizin, glabridin and licochalcone A; preferably selected from the group consisting of alpha-bisabolol, natural avenanthramides, non-natural avenanthramides, preferably dihydroavenanthramide D (as described in WO 2004 047833 A1), boswellic acid, 10
phytosterols, glycyrrhizin, and licochalcone A, and/or allantoin, panthenol, lanolin, (pseudo-)ceramides [preferably Ceramide 2, hydroxypropyl bispalmitamide MEA, cetylxypropyl glyceryl methoxypropyl myristamide, N-(1-hexadecanoyl)-4-hydroxy-L-proline (1-hexadecyl) ester, hydroxyethyl palmityl oxyhydroxypropyl palmitamide], glycosphingolipids, phytosterols, chitosan, mannose, lactose and β -glucans, in particular 1,3-1,4- β -glucan from oats.

When bisabolol is used in the context of the present invention it can be of natural or synthetic origin, and is preferably "alpha-bisabolol". Preferably, the bisabolol used is synthetically prepared or natural (-)-alpha-bisabolol and/or synthetic mixed-isomer alpha-bisabolol. If natural (-)-alpha-bisabolol is used, this can also be employed as a constituent of an essential oil or of a plant extract or of a fraction thereof, for example as a constituent of (fractions of) oil or extracts of camomile or of *Vanillosmopsis* (in particular *Vanillosmopsis erythropappa* or *Vanillosmopsis arborea*). Synthetic 30
alpha-bisabolol is obtainable, for example, under the name "Dragosantol" from Symrise.

In case ginger extract is used in the context of the present invention, preferably extracts of the fresh or dried ginger root are used which are prepared by extraction 35
with methanol, ethanol, iso-propanol, acetone, ethyl acetate, carbon dioxide (CO₂), hexane, methylene chloride, chloroform or other solvents or solvent mixtures of comparable polarity. The extracts are characterized by the presence of active skin irritation-reducing amounts of constituents such as e.g. gingerols, shogaols, gingerdiols, dehydrogingerdiones and/or paradols.

(vi) TRPV1 antagonists. Suitable compounds which reduce the hypersensitivity of skin nerves based on their action as TRPV1 antagonists, encompass e.g. trans-4-tert-butyl cyclohexanol as described in WO 2009 087242 A1, or indirect modulators of TRPV1 by an activation of the μ -receptor, e.g. acetyl tetrapeptide-15, PAR 2 antagonists, Diaryl-heptanoids and Cetearyl Nonanoate, Isononanoate, are preferred. 50

(vii) Desquamating agents. The compositions may also contain desquamating agents (component b5) in amounts of about 0.1 to about 30% b.w. preferably about 0.5 to about 15% b.w., particularly preferably about 1 to about 10% b.w. based on the total weight of the preparation. The expression "desquamating agent" is understood to mean any compound capable of acting:

either directly on desquamation by promoting exfoliation, such as β -hydroxy acids, in particular salicylic acid and its derivatives (including 5-n-octanoylsalicylic acid); α -hydroxy acids, such as glycolic, citric, lactic, tartaric, malic or mandelic acids; urea; gentisic acid; oligofucoses; cinnamic acid; extract of *Sophora japonica*; resveratrol and some derivatives of jasmonic acid; 65
or on the enzymes involved in the desquamation or the degradation of the corneodesmosomes, glycosidases,

stratum corneum chymotryptic enzyme (SCCE) or other proteases (trypsin, chymotrypsin-like). There may be mentioned agents chelating inorganic salts: EDTA; N-acyl-N,N',N'-ethylenediaminetriacetic acid; aminosulphonic compounds and in particular (N-2-hydroxyethyl)piperazine-N-2-ethane)sulphonic acid (HEPES); derivatives of 2-oxothiazolidine-4-carboxylic acid (procysteine); derivatives of alpha-amino acids of the *glycine* type (as described in EP-0 852 949, and sodium methylglycine diacetate marketed by BASF under the trade name TRILON M); honey; sugar derivatives such as O-octanoyl-6-D-maltose and N-acetylglucosamine; chestnut extracts such as those marketed by the company SILAB under the name Recoverine®, prickly pear extracts such as those marketed under the name Exfolactive® by the company SILAB, or Phytosphingosine SLC® (phytosphingosine grafted with a salicylic acid) marketed by the company Degussa.

Desquamating agents suitable for the invention may be chosen in particular from the group comprising sulphonic acids, calcium chelators, α -hydroxy acids such as glycolic, citric, lactic, tartaric, malic or mandelic acids; ascorbic acid and its derivatives such as ascorbyl glucoside and magnesium ascorbyl phosphate; nicotinamide; urea; (N-2-hydroxyethyl)piperazine-N-2-ethane)sulphonic acid (HEPES), β -hydroxy acids such as salicylic acid and its derivatives, retinoids such as retinol and its esters, retinal, retinoic acid and its derivatives, those described in the documents FR 2570377 A1, EP 0199636 A1, EP 0325540 A1, EP 0402072 A1, chestnut or prickly pear extracts, in particular marketed by SILAB; reducing compounds such as cysteine or cysteine precursors.

Desquamating agents which can be used are also nicotinic acid and its esters and nicotinamide, also called vitamin B3 or vitamin PP, and ascorbic acid and its precursors, as described in particular in application EP 1529522 A1.

(viii) Anti-cellulite agents. Anti-cellulite agents and lipolytic agents are preferably selected from the group consisting of those described in WO 2007/077541, and beta-adrenergic receptor agonists such as synephrine and its derivatives, and cyclohexyl carbamates described in WO 2010/097479. Agents enhancing or boosting the activity of anti-cellulite agents, in particular agents which stimulate and/or depolarise C nerve fibres, are preferably selected from the group consisting of capsaicin and derivatives thereof, vanillyl-nonylamid and derivatives thereof, L-carnitine, coenzym A, isoflavonoides, soy extracts, *ananas* extract and conjugated linoleic acid.

(ix) Fat enhancing agents. Formulations and products according to the present invention may also comprise one or more fat enhancing and/or adipogenic agents as well as agents enhancing or boosting the activity of fat enhancing agents. A fat enhancing agent for example hydroxymethoxyphenyl propylmethoxymethoxybenzofuran (trade name: Sym3D®).

A.14 Hair Growth Activators or Inhibitors

Formulations and products according to the present invention may also comprise one or more hair growth activators, i.e. agents to stimulate hair growth. Hair growth activators are preferably selected from the group consisting of pyrimidine derivatives such as 2,4-diaminopyrimidine-3-oxide (Aminexil), 2,4-diamino-6-piperidinopyrimidine-3-oxide (Minoxidil) and derivatives thereof, 6-amino-1,2-dihydro-1-hydroxy-2-imino-4-piperidinopyrimidine and its deriva-

tives, xanthine alkaloids such as caffeine, theobromine and theophylline and derivatives thereof, quercetin and derivatives, dihydroquercetin (taxifolin) and derivatives, potassium channel openers, antiandrogenic agents, synthetic or natural 5-reductase inhibitors, nicotinic acid esters such as tocopheryl nicotinate, benzyl nicotinate and C1-C6 alkyl nicotinate, proteins such as for example the tripeptide Lys-Pro-Val, diphencypren, hormones, finasteride, dutasteride, flutamide, bicalutamide, pregnane derivatives, progesterone and its derivatives, cyproterone acetate, spironolactone and other diuretics, calcineurin inhibitors such as FK506 (Tacrolimus, Fujimycin) and its derivatives, Cyclosporin A and derivatives thereof, zinc and zinc salts, polyphenols, procyanidins, proanthocyanidins, phytosterols such as for example beta-sitosterol, biotin, eugenol, (\pm)-beta-citronellol, panthenol, glycogen for example from mussels, extracts from microorganisms, *algae*, plants and plant parts of for example the genera dandelion (*Leontodon* or *Taraxacum*), *Orthosiphon*, *Vitex*, *Coffea*, *Paullinia*, *Theobroma*, *Asiasarum*, *Cucurbita* or *Styphnolobium*, *Serenoa repens* (saw palmetto), *Sophora flavescens*, *Pygeum africanum*, *Panicum miliaceum*, *Cimicifuga racemosa*, *Glycine max*, *Eugenia caryophyllata*, *Cotinus coggygria*, *Hibiscus rosasinensis*, *Camellia sinensis*, *Ilex paraguariensis*, *Ischraxis galbana*, *Tetraselmis suecica* licorice, grape, apple, barley or hops or/and hydrolysates from rice or wheat.

Alternatively, formulations and products according to the present invention may comprise one or more hair growth inhibitors (as described above), i.e. agents to reduce or prevent hair growth. Hair growth inhibitors are preferably selected from the group consisting of activin, activin derivatives or activin agonists, ornithine decarboxylase inhibitors such as alpha-difluoromethylornithine or pentacyclic triterpenes like for example ursolic acid, betulin, betulinic acid, oleanolic acid and derivatives thereof, 5alpha-reductase inhibitors, androgen receptor antagonists, S-adenosylmethionine decarboxylase inhibitors, gamma-glutamyl transpeptidase inhibitors, transglutaminase inhibitors, soybean-derived serine protease inhibitors, extracts from microorganisms, *algae*, different microalgae or plants and plant parts of for example the families Leguminosae, Solanaceae, Graminae, Asclepiadaceae or Cucurbitaceae, the genera *Chondrus*, *Gloiopeltis*, *Ceramium*, *Durvillea*, *Glycine max*, *Sanguisorba officinalis*, *Calendula officinalis*, *Hamelis virginiana*, *Arnica montana*, *Salix alba*, *Hypericum perforatum* or *Gymnema sylvestre*.

A.15 Cooling Agents

The compositions may also contain one or more substances with a physiological cooling effect (cooling agents), which are preferably selected here from the following list: menthol and menthol derivatives (for example L-menthol, D-menthol, racemic menthol, isomenthol, neoisomenthol, neomenthol) menthylethers (for example (1-menthoxy)-1,2-propandiol, (1-menthoxy)-2-methyl-1,2-propandiol, 1-menthyl-methylether), menthylesters (for example menthylformiate, menthylacetate, menthylisobutyrate, menthyllactates, L-menthyl-L-lactate, L-menthyl-D-lactate, menthyl-(2-methoxy)acetate, menthyl-(2-methoxyethoxy)acetate, menthylpyroglutamate), menthylcarbonates (for example menthylpropyleneglycolcarbonate, menthylethylene glycolcarbonate, menthylglycerolcarbonate or mixtures thereof), the semi-esters of menthols with a dicarboxylic acid or derivatives thereof (for example mono-menthylsuccinate, mono-menthylglutarate, mono-menthyllmalonate, O-menthyl succinic acid ester-N,N-(dimethyl)amide, O-menthyl succinic acid ester amide), menthanecarboxylic acid amides (in this case preferably menthanecarboxylic

acid-N-ethylamide [WS3] or N $^{\alpha}$ -(menthanecarbonyl)glycinethylester [WS5], as described in U.S. Pat. No. 4,150, 052, menthanecarboxylic acid-N-(4-cyanophenyl)amide or menthanecarboxylic acid-N-(4-cyanomethylphenyl)amide as described in WO 2005 049553 A1, methanecarboxylic acid-N-(alkoxyalkyl)amides), menthone and menthone derivatives (for example L-menthone glycerol ketal), 2,3-dimethyl-2-(2-propyl)-butyric acid derivatives (for example 2,3-dimethyl-2-(2-propyl)-butyric acid-N-methylamide [WS23]), isopulegol or its esters (1(-)-isopulegol, 1(-)-isopulegolacetate), menthane derivatives (for example p-menthane-3,8-diol), cubebol or synthetic or natural mixtures, containing cubebol, pyrrolidone derivatives of cycloalkyldione derivatives (for example 3-methyl-2(1-pyrrolidinyl)-2-cyclopentene-1-one) or tetrahydro-pyrimidine-2-one (for example icilene or related compounds, as described in WO 2004/026840), further carboxamides (for example N-(2-(pyridin-2-yl)ethyl)-3-p-menthanecarboxamide or related compounds), (1R,2S,5R)-N-(4-Methoxyphenyl)-5-methyl-2-(1-isopropyl)cyclohexane-carboxamide [WS12], oxamates (preferably those described in EP 2033688 A2).

A.16 Anti-Microbial Agents

Suitable anti-microbial agents are, in principle, all substances effective against Gram-positive bacteria, such as, for example, 4-hydroxybenzoic acid and its salts and esters, N-(4-chlorophenyl)-N'-(3,4-dichlorophenyl)urea, 2,4,4'-trichloro-2'-hydroxy-diphenyl ether (triclosan), 4-chloro-3, 5-dimethyl-phenol, 2,2'-methylenebis(6-bromo-4-chlorophenol), 3-methyl-4-(1-methylethyl)phenol, 2-benzyl-4-chloro-phenol, 3-(4-chlorophenoxy)-1,2-propanediol, 3-iodo-2-propynyl butylcarbamate, chlorhexidine, 3,4,4'-trichlorocarbanilide (TTC), antibacterial fragrances, thymol, thyme oil, eugenol, oil of cloves, menthol, mint oil, farnesol, phenoxyethanol, glycerol monocaprate, glycerol monocaprylate, glycerol monolaurate (GML), diglycerol monocaprate (DMC), salicylic acid N-alkylamides, such as, for example, n-octylsalicylamide or n-decylsalicylamide.

A.17 Enzyme Inhibitors

Suitable enzyme inhibitors are, for example, esterase inhibitors. These are preferably trialkyl citrates, such as trimethyl citrate, tripropyl citrate, triisopropyl citrate, tributyl citrate and, in particular, triethyl citrate (Hydagen CAT). The substances inhibit enzyme activity, thereby reducing the formation of odour. Other substances which are suitable esterase inhibitors are sterol sulfates or phosphates, such as, for example, lanosterol, cholesterol, campesterol, stigmasterol and sitosterol sulfate or phosphate, dicarboxylic acids and esters thereof, such as, for example, glutaric acid, monoethyl glutarate, diethyl glutarate, adipic acid, monoethyl adipate, diethyl adipate, malonic acid and diethyl malonate, hydroxycarboxylic acids and esters thereof, such as, for example, citric acid, malic acid, tartaric acid or diethyl tartrate, and zinc glycinate.

A.18 Odour Absorbers and Antiperspirant Active Agents

Suitable odour absorbers are substances which are able to absorb and largely retain odour-forming compounds. They lower the partial pressure of the individual components, thus also reducing their rate of diffusion. It is important that perfumes must remain unimpaired in this process. Odour absorbers are not effective against bacteria. They comprise, for example, as main constituent, a complex zinc salt of ricinoleic acid or specific, largely odour-neutral fragrances which are known to the person skilled in the art as "fixatives", such as, for example, extracts of *labdanum* or *styrax* or certain abietic acid derivatives. The odour masking agents are fragrances or perfume oils, which, in addition to their

function as odour masking agents, give the deodorants their respective fragrance note. Perfume oils which may be mentioned are, for example, mixtures of natural and synthetic fragrances. Natural fragrances are extracts from flowers, stems and leaves, fruits, fruit peels, roots, woods, herbs and grasses, needles and branches, and resins and balsams. Also suitable are animal products, such as, for example, civet and castoreum. Typical synthetic fragrance compounds are products of the ester, ether, aldehyde, ketone, alcohol, and hydrocarbon type. Fragrance compounds of the ester type are, for example, benzyl acetate, p-tert-butylcyclohexyl acetate, linalyl acetate, phenylethyl acetate, linalyl benzoate, benzyl formate, allyl cyclohexylpropionate, styrallyl propionate and benzyl salicylate. The ethers include, for example, benzyl ethyl ether, and the aldehydes include, for example, the linear alkanals having 8 to 18 carbon atoms, citral, citronellal, citronellyloxyacetaldehyde, cyclamen aldehyde, hydroxycitronellal, lilyal and bourgeonal, the ketones include, for example, the ionones and methyl cedryl ketone, the alcohols include anethole, citronellol, eugenol, isoeugenol, geraniol, linalool, phenylethyl alcohol and terpineol, and the hydrocarbons include mainly the terpenes and balsams. Preference is, however, given to using mixtures of different fragrances which together produce a pleasing fragrance note. Essential oils of relatively low volatility, which are mostly used as aroma components, are also suitable as perfume oils, e.g. sage oil, camomile oil, oil of cloves, *melissa* oil, mint oil, cinnamon leaf oil, linden flower oil, juniperberry oil, vetiver oil, olibanum oil, *galbanum* oil, *labdanum* oil and lavandin oil. Preference is given to using bergamot oil, dihydromyrcenol, lilyal, lylal, citronellol, phenylethyl alcohol, α -hexylcinnamaldehyde, geraniol, benzylacetone, cyclamen aldehyde, linalool, boisambrene forte, ambroxan, indole, hedione, sandelice, lemon oil, mandarin oil, orange oil, allyl amyl glycolate, cyclovertal, lavandin oil, clary sage oil, β -damascone, geranium oil bourbon, cyclohexyl salicylate, Vertofix coeur, iso-E-super, Fixolide NP, evernyl, iraldein gamma, phenylacetic acid, geranyl acetate, benzyl acetate, rose oxide, romilat, irotyl and floramat alone or in mixtures; talcum.

Suitable astringent antiperspirant active ingredients are primarily salts of aluminium, zirconium or of zinc. Such suitable antihydrotic active ingredients are, for example, aluminium chloride, aluminium chlorohydrate, aluminium dichlorohydrate, aluminium sesquichlorohydrate and complex compounds thereof, e.g. with 1,2-propylene glycol, aluminium hydroxyallantoinate, aluminium chloride tartrate, aluminium zirconium trichlorohydrate, aluminium zirconium tetrachlorohydrate, aluminium zirconium pentachlorohydrate and complex compounds thereof, e.g. with amino acids, such as *glycine*.

A.19 Film Formers and Anti-Dandruff Agents

Standard film formers are, for example, chitosan, microcrystalline chitosan, quaternized chitosan, polyvinyl pyrrolidone, vinyl pyrrolidone/vinyl acetate copolymers, polymers of the acrylic acid series, quaternary cellulose derivatives, collagen, hyaluronic acid and salts thereof and similar compounds.

Suitable antidandruff agents are Pirocton Olamin (1-hydroxy-4-methyl-6-(2,4,4-trimethyl-pentyl)-2-(1H)-pyridine monoethanolamine salt), Climbazole, Ketoconazol® (4-acetyl-1-{4-[2-(2,4-dichlorophenyl) r-2-(1H-imidazol-1-ylmethyl)-1,3-dioxylan-c-4-ylmethoxyphenyl]}-piperazine, ketoconazole, elubiol, selenium disulfide, colloidal sulfur, sulfur polyethylene glycol sorbitan monooleate, sulfur ricinol polyethoxylate, sulfur tar distillate, salicylic acid (or in combination with hexachlorophene), undecylenic acid,

monoethanolamide sulfosuccinate Na salt, Lamepon® UD (protein/undecylenic acid condensate), zinc pyrithione, aluminium pyrithione and magnesium pyrithione/dipyrithione magnesium sulfate.

5 A.20 Carriers and Hydrotropes

Preferred cosmetics carrier materials are solid or liquid at 25° C. and 1013 mbar (including highly viscous substances) as for example glycerol, 1,2-propylene glycol, 1,2-butylene glycol, 1,3-propylene glycol, 1,3-butylene glycol, ethanol, 10 water and mixtures of two or more of said liquid carrier materials with water. Optionally, these preparations according to the invention may be produced using preservatives or solubilizers. Other preferred liquid carrier substances, which may be a component of a preparation according to the invention are selected from the group consisting of oils such as vegetable oil, neutral oil and mineral oil, butter.

Preferred solid carrier materials, which may be a component of a preparation according to the invention are hydrocolloids, such as starches, degraded starches, chemically or 20 physically modified starches, dextrans, (powdery) maltodextrins (preferably with a dextrose equivalent value of 5 to 25, preferably of 10-20), lactose, silicon dioxide, glucose, modified celluloses, gum arabic, ghatti gum, tragacanth, karaya, carrageenan, pullulan, curdlan, xanthan gum, gellan gum, guar flour, carob bean flour, alginates, agar, pectin and inulin and mixtures of two or more of these solids, in particular 25 maltodextrins (preferably with a dextrose equivalent value of 15-20), lactose, silicon dioxide and/or glucose.

In addition, hydrotropes, for example ethanol, isopropyl alcohol or polyols, may be used to improve flow behaviour. Suitable polyols preferably contain 2 to 15 carbon atoms and at least two hydroxyl groups. The polyols may contain other functional groups, more especially amino groups, or may be modified with nitrogen. Typical examples are

- glycerol;
- alkylene glycols such as, for example, ethylene glycol, diethylene glycol, propylene glycol, butylene glycol, hexylene glycol and polyethylene glycols with an average molecular weight of 100 to 1000 Dalton;
- 40 technical oligoglycerol mixtures with a degree of self-condensation of 1.5 to 10, such as for example technical diglycerol mixtures with a diglycerol content of 40 to 50% by weight;
- methylol compounds such as, in particular, trimethylol ethane, trimethylol propane, trimethylol butane, pentaerythritol and dipentaerythritol;
- lower alkyl glucosides, particularly those containing 1 to 8 carbon atoms in the alkyl group, for example methyl and butyl glucoside;
- 50 sugar alcohols containing 5 to 12 carbon atoms, for example sorbitol or mannitol,
- sugars containing 5 to 12 carbon atoms, for example glucose or sucrose;
- amino sugars, for example glucamine;
- 55 dialcoholamines, such as diethanolamine or 2-aminopropane-1,3-diol.

A.21 Preservatives

Suitable preservatives are, for example, phenoxyethanol, formaldehyde solution, parabens, pentanediol or sorbic acid and the other classes of compounds listed in Appendix 6, Parts A and B of the Kosmetikverordnung ("Cosmetics Directive"), acetophenones, glycerylethers.

A.22 Perfume Oils and Fragrances

Suitable perfume oils are mixtures of natural and synthetic perfumes. Natural perfumes include the extracts of blossoms (lily, lavender, rose, jasmine, neroli, ylang-ylang), stems and leaves (geranium, patchouli, petitgrain), fruits

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(anise, coriander, caraway, juniper), fruit peel (bergamot, lemon, orange), roots (nutmeg, *angelica*, celery, cardamom, costus, iris, calmus), woods (pinewood, sandalwood, guaiac wood, cedarwood, rosewood), herbs and grasses (tarragon, lemon grass, sage, thyme), needles and branches (spruce, fir, pine, dwarf pine), resins and balsams (*galbanum*, elemi, benzoin, myrrh, olibanum, opoponax). Animal raw materials, for example civet and beaver, may also be used. Typical synthetic perfume compounds are products of the ester, ether, aldehyde, ketone, alcohol and hydrocarbon type. Examples of perfume compounds of the ester type are benzyl acetate, phenoxyethyl isobutyrate, p-tert.butyl cyclohexylacetate, linalyl acetate, dimethyl benzyl carbonyl acetate, phenyl ethyl acetate, linalyl benzoate, benzyl formate, ethylmethyl phenyl glycinate, allyl cyclohexyl propionate, styrallyl propionate and benzyl salicylate. Ethers include, for example, benzyl ethyl ether while aldehydes include, for example, the linear alkanals containing 8 to 18 carbon atoms, citral, citronellal, citronellyloxyacetaldehyde, cyclamen aldehyde, hydroxycitronellal, linal and bourgeonal. Examples of suitable ketones are the ionones, α -isomethylionone and methyl cedryl ketone. Suitable alcohols are anethol, citronellol, eugenol, isoeugenol, geraniol, linalool, phenylethyl alcohol and terpineol. The hydrocarbons mainly include the terpenes and balsams. However, it is preferred to use mixtures of different perfume compounds which, together, produce an agreeable perfume. Other suitable perfume oils are essential oils of relatively low volatility which are mostly used as aroma components. Examples are sage oil, camomile oil, clove oil, *melissa* oil, mint oil, cinnamon leaf oil, lime-blossom oil, juniper berry oil, vetiver oil, olibanum oil, *galbanum* oil, *ladanum* oil and lavandin oil. The following are preferably used either individually or in the form of mixtures: bergamot oil, dihydro-myrcenol, linal, lylal, citronellol, phenylethyl alcohol, hexylcinnamaldehyde, geraniol, benzyl acetone, cyclamen aldehyde, linalool, Boisambrene Forte, Ambroxan, indole, hedione, sandelice, citrus oil, mandarin oil, orange oil, allylamyl glycolate, cyclovertal, lavandin oil, clary oil, damascone, geranium oil bourbon, cyclohexyl salicylate, Vertofix Coeur, Iso-E-Super, Fixolide NP, evermyl, iraldein gamma, phenylacetic acid, geranyl acetate, benzyl acetate, rose oxide, romillat, irotyl and floramat.

A.23 Dyes

Suitable dyes are any of the substances suitable and approved for cosmetic purposes as listed, for example, in the publication "*Kosmetische Färbemittel*" of the Farbstoffkommission der Deutschen Forschungsgemeinschaft, Verlag Chemie, Weinheim, 1984, pages 81 to 106. Examples include cochineal red A (C.I. 16255), patent blue V (C.I. 42051), indigotin (C.I. 73015), chlorophyllin (C.I. 75810), quinoline yellow (C.I. 47005), titanium dioxide (C.I. 77891), indanthrene blue RS (C.I. 69800) and madder lake (C.I. 58000). Luminol may also be present as a luminescent dye. Advantageous coloured pigments are for example titanium dioxide, mica, iron oxides (e.g. Fe_2O_3 , Fe_3O_4 , FeO (OH)) and/or tin oxide. Advantageous dyes are for example carmine, Berlin blue, chromium oxide green, ultramarine blue and/or manganese violet.

A.24 Preparations

Preferred compositions according to the present inventions are selected from the group of products for treatment, protecting, care and cleansing of the skin and/or hair or as a make-up product, preferably as a leave-on product (meaning that the one or more compounds of formula (I) stay on the skin and/or hair for a longer period of time, compared to

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rinse-off products, so that the moisturizing and/or anti-ageing and/or wound healing promoting action thereof is more pronounced).

The formulations according to the invention are preferably in the form of an emulsion, e.g. W/O (water-in-oil), O/W (oil-in-water), W/O/W (water-in-oil-in-water), O/W/O (oil-in-water-in-oil) emulsion, PIT emulsion, Pickering emulsion, emulsion with a low oil content, micro- or nanoemulsion, a solution, e.g. in oil (fatty oils or fatty acid esters, in particular C_6 - C_{32} fatty acid C_2 - C_{30} esters) or silicone oil, dispersion, suspension, creme, lotion or milk, depending on the production method and ingredients, a gel (including hydrogel, hydrodispersion gel, oleogel), spray (e.g. pump spray or spray with propellant) or a foam or an impregnating solution for cosmetic wipes, a detergent, e.g. soap, synthetic detergent, liquid washing, shower and bath preparation, bath product (capsule, oil, tablet, salt, bath salt, soap, etc.), effervescent preparation, a skin care product such as e.g. an emulsion (as described above), ointment, paste, gel (as described above), oil, balsam, serum, powder (e.g. face powder, body powder), a mask, a pencil, stick, roll-on, pump, aerosol (foaming, non-foaming or post-foaming), a deodorant and/or antiperspirant, mouthwash and mouth rinse, a foot care product (including keratolytic, deodorant), an insect repellent, a sunscreen, aftersun preparation, a shaving product, aftershave balm, pre- and aftershave lotion, a depilatory agent, a hair care product such as e.g. shampoo (including 2-in-1 shampoo, anti-dandruff shampoo, baby shampoo, shampoo for dry scalps, concentrated shampoo), conditioner, hair tonic, hair water, hair rinse, styling creme, pomade, perm and setting lotion, hair spray, styling aid (e.g. gel or wax), hair smoothing agent (detangling agent, relaxer), hair dye such as e.g. temporary direct-dyeing hair dye, semi-permanent hair dye, permanent hair dye, hair conditioner, hair mousse, eye care product, make-up, make-up remover or baby product.

The formulations according to the invention are particularly preferably in the form of an emulsion, in particular in the form of a W/O, O/W, W/O/W, O/W/O emulsion, PIT emulsion, Pickering emulsion, emulsion with a low oil content, micro- or nanoemulsion, a gel (including hydrogel, hydrodispersion gel, oleogel), a solution e.g. in oil (fatty oils or fatty acid esters, in particular C_6 - C_{32} fatty acid C_2 - C_{30} esters) or silicone oil, or a spray (e.g. pump spray or spray with propellant).

Auxiliary substances and additives can be included in quantities of 5 to 99% b.w., preferably 10 to 80% b.w., based on the total weight of the formulation. The amounts of cosmetic or dermatological auxiliary agents and additives and perfume to be used in each case can easily be determined by the person skilled in the art by simple trial and error, depending on the nature of the particular product.

The preparations can also contain water in a quantity of up to 99% b.w., preferably 5 to 80% b.w., based on the total weight of the preparation.

INDUSTRIAL APPLICATION

Another object of the present invention refers to a non-therapeutic method for increasing hair growth in general, and increasing hair shaft elongation and density of eyelashes and eyebrows in particular, by topical administration of the mixture of components (a) and (b) or the composition comprising said mixture to human scarp or skin.

Finally, the invention encompasses the use of the mixture of components (a) and (b) or the composition comprising

said mixture for increasing hair growth, in particular for increasing hair shaft elongation and density of eyelashes and eyebrows.

EXAMPLES

Examples 1 to 3, Comparative Examples C1 to C4

In-vivo studies were conducted with a panel of 10 subjects. Serum comprising the actives in different concentrations was applied once a day in the evening using an eyelash brush at the roots of the lashes. The duration of the study was 6 weeks; evaluation took place after 14, 28 and 42 days. Eyelash density and eyelash volume, distal length and width were evaluated using high resolution reverse photo engineering. The results as the average of values from the left and the right eyelash are reported in Table 1. Examples 1 to 4 are according to the invention, examples C1 to C4 serve for comparison.

TABLE 1

Improvement in eyelash density compared to baseline at day 0					
Ex.	Serum	14 d	28 d	42 d	
C1	2% Sympeptide ® XLash ¹⁾	+2.3%	+4.5%	+9.0%	
1	2% Sympeptide ® XLash + 0.1% Troxerutin	+9.5%	+15.1%	+22.2%	
C2	5% Sympeptide ® XLash	+8.5%	+34.4%	+42.5%	
2	5% Sympeptide ® XLash + 0.1% Troxerutin	+16.5%	+42.6%	+49.7%	
C3	10% Sympeptide ® XLash	+31.2%	+52.5%	+64.5%	
3	10% Sympeptide ® XLash + 0.1% Troxerutin	+35.7%	+59.8%	+71.0%	
C4	2% Widelash ® ²⁾	+6.0%	+12.2%	+16.1%	
4	2% Widelash ® + 0.1% Troxerutin	+9.5%	+14.2%	+20.2%	

¹⁾myristoyl pentapeptide-17 (Symrise AG)

²⁾Biotinoyl tripeptide-1 (Sederma)

The examples and comparative examples clearly demonstrate the boosting effect of troxerutin on the acylated oligopeptides. The highest relative increase is found at lower concentrations, indicating that the synergistic mixture leads to a significant improvement even when used in much lower concentrations as it is usual until today. Therefore, the problem underlying the present invention is fully solved.

The following Tables 2 and 3 show formulation examples for the purpose to illustrate the invention in more detail.

TABLE 2

Eyelash serum (amounts in % b.w.)			
Phase	Ingredients	INCI Name	Amount
A	Water	Aqua	Ad 100
	Natrosol ® 250 HHR	Hydroxyethylcellulose	0.500
	Symdiol ® 68T	1,2-Hexanediol, Caprylyl Glycol, Tropolone	0.500
	Sodium Chloride	Sodium Chloride	0.500
	Lactic Acid	Lactic acid	0.100
	Sodium Borate	Sodium Borate	0.150
	Edeta ® BD	Disodium EDTA	0.100
	Biotive ® Troxerutin	Troxerutin	0.100
	SymPeptide ® XLash	Water, Glycerin, Myristoyl Pentapeptide-17	2.000

To obtain the formulation dispense Natrosol® into water and heat up to 60° C. while stirring. Let cool down to 40° C. while stirring and add the remaining ingredients of phase A. Add phase B while stirring. Check that pH is around 7.

TABLE 3

Mascara (amounts in % b.w.)			
Phase	Ingredients	INCI Name	Amount
A	Water	Aqua	Ad 100
	Solagum ® AX	Acacia Senegal, Xanthan gum	0.300
	Hydrolyte ® 5	Pentylene Glycol	1.000
	Emulsiphos ®	Potassium Cetyl Phosphate	2.500
	Food Color Iron Oxide	Iron Oxides	10.000
	Ronaflair ® M-Sphere	Mica	2.000
	SymTriol ®	Caprylyl Glycol, 1,2-Hexandiol, Methylbenzyl Alcohol	0.800
	PCL-Liquid 100	Cetearyl Ethylhexanoate	2.000
	Dragoxat ® 89	Ethylhexyl Isononaote	2.000
B	Cutina ® GMS-V	Glyceryl Stearate	3.5000
	Beeswax	Beeswax	5.500
	Syncrowax ® NRC	Tribehenin	3.000
	Controx ® Ks	Tocopherol, Hydrogenated PUalm Glycerides Citrate	0.1000
	Xiameter ® PMX-200	Dimethicone	0.200
	Silicone		
	SymPeptide ® XLash	Water, Glycerin, Myristoyl Pentapeptide-17	1.000
	Biotive ® Troxerutin	Troxerutin	0.080
	Luvissette ® Clear	VP/Methacrylamide/Vinyl Imidazole Copolymer	20.000
C	Hydromoiest ® O	Water, Avena Sativa Peptide	1.00

To obtain phase A heat water and Hydrolite to 85° C., dissolve Solagum® AX while stirring, add and dissolve Emulsiphos®, add and dispese the pigments and finally add SymTriol®. For phase B mix all ingredients and heat to 85° C. Emulsify phase B to phase A while stirring and homogenize. Cool to 40 to 45° C. while stirring. Add phase C and cool to room temperature. Check that pH value is about 6.5.

The invention claimed is:

1. An active mixture of comprising:

(a) myristoyl pentapeptide-17, and

(b) troxerutin,

wherein components (a) and (b) are present in a ratio by weight of from about 1:99 to about 99:1.

2. The mixture of claim 1, wherein components (a) and (b) are present in a ratio by weight of from about 80:20 to about 98:2.

3. A medicament comprising the mixture of claim 1 in an amount effective for potentiating hair growth.

4. A medicament comprising the mixture of claim 1 in an amount effective for potentiating hair shaft elongation.

5. A medicament comprising the mixture of claim 1 in an amount effective for potentiating density of eyelashes and eyebrows.

6. A method for increasing hair growth in a subject, comprising the step of topically administering the active mixture of claim 1 to the subject's scalp or skin.

7. A method to increase hair shaft elongation and density of eyelashes and eyebrows in a subject, comprising the step of topically administering the active mixture of claim 1 to the subject's scalp or skin.

8. A cosmetic or dermatological composition comprising the active mixture of claim 1.

9. The composition of claim 8, comprising said active mixture in an amount of from about 0.01 to about 5% by weight.

10. The composition of claim 9, comprising said active mixture in an amount of from about 0.1 to about 2% by weight.

11. The composition of claim 8, wherein said composition is in the form of an eyelash conditioner and further comprises a cosmetically or dermatologically acceptable carrier.

12. The composition of claim 11, further comprising
 (c) at least one ingredient selected from the group consisting of acacia senegal, xanthan gum, pentylene glycol, potassium cetyl phosphate, iron oxide, mica, caprylyl glycol, 1,2-hexandiol, methylbenzyl alcohol, 5
 ceteary ethylhexanoate, ethylhexyl isononaote, glyceryl stearate, beeswax, tribehenin, tocopherol, hydrogenated glycerides citrate, dimethicone, VP/Methacrylamide/vinyl imidzaole copolymer and avena sativa peptide. 10

13. A medicament comprising the composition of claim 8 in an amount effective for potentiating hair growth.

14. A medicament comprising the composition of claim 8 in an amount effective for potentiating hair shaft elongation.

15. A medicament comprising the composition of claim 8 in an amount effective for potentiating density of eyelashes and eyebrows. 15

16. A method for increasing hair growth in a subject, comprising the step of topically administering the composition of claim 8 to the subject's scalp or skin. 20

17. A method to increase hair shaft elongation and density of eyelashes and eyebrows in a subject, comprising the step of topically administering the composition of claim 8 to the subject's scalp or skin. 25

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