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(54) **Title:** USE OF AGENTS SUCH AS NONPOLYMERIC NITRIC OXIDE DONORS FOR MAKING THE LIPS FULL AGAIN AND/OR COLOURING THE LIPS

(57) **Abstract:** The invention relates in particular to the cosmetic use (i) of at least one agent for promoting the production of NO in and/or on the lips, chosen from nitric oxide NO donors or precursors; nonpolymeric NO releasers; and NO synthase synthesis and/or activity stimulators; or (ii) of other agents for promoting microcirculation in the skin, chosen from potassium channel openers; calcium channel blockers; phosphodiesterase inhibitors; flavonoids; vasodilator peptides that are not NO donors; temperature modulators; agents for promoting the stimulation and/or maintenance of angiogenesis; agents for promoting the stimulation of endothelial cell proliferation; agents for promoting endothelial cell migration; and mixtures thereof, in a makeup and/or care composition for the lips, as an agent for naturally making the lips full again and/or naturally coloring the lips. It also relates to specific care and/or makeup compositions for the lips containing said agent, and also to a cosmetic process aimed at making the lips naturally full and/or colored, using said compositions .

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USE OF AGENTS SUCH AS NONNPOLYMERIC NITRIC OXYDE DONORS FOR MAKING THE LIPS FULL AGAIN AND/OR COLOURING THE LIPS

The field of the invention relates to lipcare and/or making up the lips, in particular naturally making up the lips.

The term "naturally making up" the lips is intended to mean, according to the invention, a means for naturally colouring the lips and/or naturally making the lips full again, as opposed to conventional making up of the lips, which uses makeup agents such as dyes, specific pigments or reflecting particles capable of conferring an optical effect of coloration and/or of volume (fullness effect) of the lips.

The term "naturally colouring" is intended to mean, according to the invention, stimulating the naturally pinkish coloration of the lips.

The term "making the lips full again" is intended to mean, according to the invention, increasing the size and/or the volume and/or the thickness of the lips and/or remodelling them and/or smoothing them and/or giving them a plumper or fleshier appearance.

The invention relates in particular to the cosmetic use (i) of at least one agent for promoting the production of NO in and/or on the lips chosen from

nitric oxide (NO) donors or precursors; nonpolymeric NO releasers; and NO synthase synthesis and/or activity stimulators; or (ii) of other agents for promoting microcirculation in the skin, chosen from potassium channel openers; calcium channel blockers; phosphodiesterase inhibitors; flavonoids; vasodilator peptides that are not NO donors; temperature modulators; agents for promoting the stimulation and/or maintenance of angiogenesis; agents for promoting the stimulation of endothelial cell proliferation; agents for promoting endothelial cell migration; and mixtures thereof, as a makeup and/or care composition for the lips, as an agent for naturally making the lips full again and/or naturally colouring the lips.

It also relates to specific care and/or makeup compositions for the lips containing said agent, and also to a cosmetic process aimed at making the lips naturally coloured and/or full, using said compositions.

Thin lips, in particular in women, are considered to be unattractive. To increase the thickness of the lips, women in particular have recourse to cosmetic surgery, injection and tattooing techniques, and the use of these techniques has a tendency to become generalized, including in women with normal lips, who desire fleshy or full lips. However, these techniques are expensive, and can, for some, give

an irreversible result (for example, cosmetic surgery, tattooing) or, for others, generate side effects such as infection or allergy (for example, injection of collagen, tattooing, etc).

As more cosmetic alternative solutions, the applicant has in particular proposed, in application EP 1 382 323, the use, in a composition for the lips, of at least one goniochromatic colouring agent able to create a goniochromatic coloured background which changes according to the angle of observation and/or of incidence of the light, combined with reflective particles able to create, when the composition is applied to the lips, highlight points that create an optical effect of volume or fullness effect.

The use of mixtures of agents chosen from (i) local vasodilators such as beta-adrenergic receptor blockers or muscarinic acetylcholine receptor activators, (ii) local irritants, and (iii) homeopathic-dose elements, for augmenting the size of the lips is also known in patent US 5,571,794.

More recently, application WO 03/072039 describes compositions containing a polymer of 7 to 15 L-arginine units, for increasing the size of keratin materials such as the skin, the hair, the lips and the gums.

However, there remains the need to find effective agents for naturally making up the lips, in

particular agents capable of naturally colouring the lips and/or naturally making the lips full again, which is cosmetically acceptable and can be formulated in compositions for topical application to the lips.

The applicant proposes using an agent for promoting the production of nitric oxide NO in and/or on the lips, chosen from nitric oxide NO donors or precursors; nonpolymeric NO releasers; and NO synthase synthesis and/or activity stimulators, in order to satisfy this need.

The term "nonpolymeric NO releasers" is intended to mean, according to the invention, any NO-releasing agent that is peptide or nonpeptide in nature, it being understood that, when the agent is peptide in nature, it comprises from 1 to 5 amino acids, preferably from 2 to 4 amino acids.

Nitric oxide is known to be involved in many biological processes, in particular in the immune system, and it has many interactions with nucleic acid, proteins, low molecular weight thiols, etc. The applicant has already proposed the use of NO donors or precursors in cosmetic or dermatological compositions, in the fields of skin or mucous membrane vascularization, of bacterial growth regulation, of the prevention of damage caused by UV radiation, of slimming, of anti-ageing, etc. Because of its gaseous state, NO also has the advantage of readily diffusing

over the skin or the lips or in the superficial layers of the skin or the lips, making it possible to rapidly obtain the desired effect.

According to one alternative, it is also possible to use, according to the invention, other agents for promoting microcirculation in the skin which act, after topical application to the lips, (i) via a stimulation of vasodilation and/or an anticoagulant effect and/an antihypertensive effect, and/or (ii) via a stimualtion and/or the maintenance of angiogenesis, and/or (iii) via a stimulation of endothelial cell proliferation, and/or (iv) a stimulation of endothelial cell migration.

In particular, as agents which act via (i) a stimulation of vasodilation and/or an anticoagulant effect and/or an antihypertensive effect, mention may be made of:

- antihypertensive agents; in particular, potassium channel openers;
- phosphodiesterase inhibitors;
- flavonoids or flavoglycosides;
- glucosides;
- plant extracts with vasodilator properties;
- vasodilator peptides that are not NO donors;
- other vasodilators;
- temperature modulators.

NO donors or precursors

As NO donors, mention may in particular be made of organic compounds which give NO by chemical reaction comprising a nitro ($-NO_2$) or nitroso (-NO) substituent, oximes, heterocyclic NO donors, compounds that give nitroxyl, hydroxylamine, nonoate compounds ($-N(NO)O^-$), *N*-hydroxyguanidine and its salts (hemisulphate HG, or acetate NOHA), inorganic NO donors, transition metals-nitrosyl, nitrosodiphenylamine derivatives, the cyclosine from the Thissen laboratories, SMP-5185 or N-nitratopivaloyl-S-(N'-acetylalanyl)cysteine ethyl ester from the Schwarz Pharma laboratories, photolabile NO donors, guanylate cyclase activators and/or cGMP stimulators, molecules developed by the company Nicox, such as NO-fluorbiprofen (HCT 1026), NO-hydrocortisone (NCX 1022) and NO-aspirin (NCX 4016).

Among the organic compounds comprising a nitro ($-NO_2$) or nitroso (-NO) substituent, mention may be made of:

- compounds comprising a nitro or nitroso substituent linked to a carbon atom (C-nitro, C-nitroso), such as 2-methyl-2-nitrosopropane (MNP),
- compounds comprising a nitro or nitroso substituent linked to a sulphur atom (S-nitro, S-nitroso), such as *S*-nitroso-*N*-acetyl-D,L-penicillamine (SNAP), *S*-nitrosoglutathione (SNOG), *N*-acetyl-*S*-nitrosopenicillaminyl-*S*-nitrosopenicillamine,

thionitrates or thionitrites (S-nitrosothiols),
- compounds comprising a nitro or nitroso substituent linked to an oxygen atom (O-nitroso), such as, for example, glyceryl trinitrate (GTN) or nitroglycerine, isosorbide dinitrate (ISDN), isosorbide 5-mononitrate (IS-5-N), isopropyl nitrate, isobutyl nitrate, isopentyl nitrate, ethylene glycol dinitrate, glyceryl 1-mononitrate, glyceryl 1,2-dinitrate, glyceryl 1,3-dinitrate, butane-1,2,4-triol trinitrate, erythrityl tetranitrate, pentaerythrityl tetranitrate, and organic nitrites such as ethyl nitrite, isobutyl nitrite or isopentyl nitrite (amyl nitrite),
- compounds comprising a nitro or nitroso substituent linked to a nitrogen atom (N-nitroso), such as *N*-nitrosodimethylamine (NDMA), N-methyl-*N*-nitrosourea (MNU), 1,3-bis-(2-chloroethyl)-1-nitrosourea (BCNU), 1-methyl-3-nitro-1-nitrosoguanidine (MNNG), streptozotocine (STZ), *N*-nitroso-*N*-phenylhydroxylamine, *N*-nitrosamines, *N*-hydroxy-*N*-nitrosamines, *N*-nitrosamides, *N*-nitrosoguanidines, *N*-nitrosohydrazines, or *N*-nitrosimines.

Among the nonoate compounds, mention may in particular be made of spermine (Sper/NO), diethylamine (DEA/NO), diethylenetriamine (DETA/NO, NOC-18), *N,N'*-bismethyl-1,6-hexenediamine (MAMA/NO, NOC-9), *N*-propyl-1,3-propanediamine (PAPA/NO, NOC-15), *N*-isopropyl-1,3-propanediamine (NOC-5), *N,N'*-bismethyl-1,3-

propanediamine (NOC-7), *N,N'*-bisethylethylenediamine INOC-12), 1-{[4',5'-bis(carboxymethoxy)-2'-nitrophenyl]methoxy}-2-oxo-3,3-diethyl-1-triazine (CNO-4), or 1-{[4',5'-bis(carboxymethoxy)-2'-nitrophenyl)methoxy}-2-oxo-3,3-diethyltriazine (CNO-5).

Among the oximes, mention may, for example, be made of:

- (±)-[(E)-ethyl-2-[(E)-hydroxyimino]-5-nitro-3-hexeneamide] (KF409, NOR-3),
- (±)-*N*-[(E)-4-ethyl-3-[(Z)-hydroxyimino]-5-nitro-3-hexen-1-yl]-3-pyridinecarboxamide (FR144420, NOR-4).

Among the heterocyclic NO-donor compounds, mention may in particular be made of:

- sydnonimines, such as molsidomine (MOL), 3-morpholinosydnonimine (linsidomine, SIN-1), the *N*-morpholino-*N*-nitrosaminoacetonitrile/γ-cyclodextrin complex (SIN-1A/gamma-CD),
- oxadiazoles (furoxanes) such as 4-phenyl-3-furoxancarbonitrile,
- oxatriazoles, such as [1,2,3,4-oxatriazolium-5-amino-3-(3,4-dichlorophenyl)] chloride (GEA 3162), [1,2,3,4-oxatriazolium-5-amino-3-(3-chloro-2-methylphenyl)] chloride (GEA 5024), [1,2,3,4-oxatriazolium-3-(3-chloro-2-methylphenyl)-5-[cyanomethylamino]carboxamido] hydroxide (GEA5583), and
- diazetidine-di-*N*-oxide.

Among the compounds bearing a nitroxyl substituent ($-NO^-$), mention may be made of: benzenesulphohydroxamic acid (Piloty's acid, PA, BSHA), *N*-acetyl-*N*-acetoxy-4-chlorobenzenesulphonamide, cyanamide, sodium trioxodinitrate (Angeli's salt) and sodium nitroxyl.

Among the inorganic NO-donor compounds, mention may in particular be made of nitrosonium salts, nitrosyl halides, nitrite salts, sodium nitrite ($NaNO_2$), nitrosyl hydrogen sulphate ($NOHSO_4$), nitrosyl chloride (NOCl), nitrosyl tetrafluoroborate ($NOBF_4$), peroxynitrite ($ONOO^-$) and sodium azide (NaN_3). Mention may also be made of inorganic nitrites associated with organic acids, such as ascorbic acid or salicylic acid, as described in application WO 99/44622.

Among the transition metal complexes with nitrosyl ($-NO^+$) as a ligand, mention may in particular be made of dinitrosyl-iron(II) complexes, complexes of nitrosyl with iron-sulphur clusters, complexes of nitrosyl with other transition metals, sodium nitroprusside (SNP, $Na_2[Fe(CN)_5NO]$), the dinitrosyl-iron-cysteine complex (1:20) (DNIC) and pentachloronitrosylruthenium ($K_2[Ru(NO)Cl_5]$).

Among the photolabile NO donors, mention may in particular be made of the compounds:

- N,N'-dimethyl-N,N'-dinitroso-p-phenylenediamine (BNN3);

- N,N'-dicarboxymethyl-N,N'-dinitroso-p-phenylenediamine, 2Na (BNN5Na);
- N,N'-dinitroso-p-phenylenediamine-N,N'-diacetic acid dimethyl ester (BNN5 methyl ester).

Among the "guanylate cyclase activators and/or cGMP stimulators", mention may in particular be made of atrial natriuretic factor and S-nitroso-N-acetylpenicillamine (SNAP).

The agents for modulating NO synthesis can act directly on the chemical release of NO, or on the enzymatic release of NO by means of the enzyme for synthesizing NO, NO synthase or NOS (its various isoforms). Reference will in particular be made, in the description, to "NO releasers", and in particular "nonpolymeric NO releasers", i.e. any NO-releasing agent that is peptide or nonpeptide in nature, it being understood that, when the agent is peptide in nature, it comprises from 1 to 5 amino acids, preferably from 2 to 4 amino acids.

They can also be elements that ultimately regulate the concentration of NO at the cellular level, by acting on the mechanisms of protein synthesis of the enzyme, on the stability and/or the activity of the enzyme and also on the stimulation of the synthesis thereof, on the stability of the NOS mRNA, on the stability of the released NO. Reference will in

particular be made, in the description, to "NOS synthesis and/or activity stimulators".

Finally, certain interactions at the level of the NO metabolism, upstream of the synthesis thereof, can interfere with the final concentration of released NO, by acting on the other enzymes that have the same substrate, on the availability of the substrate at the intracellular level, and on its transport within the cell.

The term "NO synthase" covers a family of enzymes that carry out the enzymatic catalysis of L-arginine to citrulline, during which catalysis a gaseous mediator with multiple functions, nitric oxide or NO, is produced.

NO synthases exist in three forms, two constitutive forms, which nomenclature groups together neuronal NO synthase (or NOS 1) and endothelial NO synthase (or NOS 3) and the inducible form (or NOS 2) (Medicine/Sciences, 1992, 8, pp. 843-845).

Nonpolymeric NO releasers

As examples, mention may in particular be made of amino acids, peptides, the proanthocyanidines as described in application JP2001-278792, and the cyclic terpenes described in application WO 00/044368, it being understood that the peptides used according to the invention will comprise from 1 to 5 amino acids, preferably from 2 to 4 amino acids.

Among the amino acids that stimulate NO release by enzymatic action, mention may be made of L-arginine, histidine, lysine, ornithine, glutamic acid, aspartic acid, serine, glycine, cysteine and threonine. Basic, acidic or alcoholic aliphatic amino acids are preferred.

Mention may in particular be made of peptides having from 1 to 5 amino acids, preferably from 2 to 4 amino acids, chosen from:

- L-arginine oligomers, oligomers of an L-arginine analogue or of one of their derivatives, such as those described by Exsymol in application EP 1 060 739, the content of which is incorporated into the present application by way of reference,
- histidine- and/or alanine-based peptides described by KS Biomedix Ltd in application WO 02/04005, the content of which is incorporated into the present application by way of reference, in particular histidine dipeptides such as carnosine, anserine and homocarnosine.

Mention may also be made of the compounds developed by the company Nitromed, such as the COX-2 inhibitors that stimulate NO production, the PDE inhibitors that stimulate NO production, the steroids that stimulate NO production, the arginines that

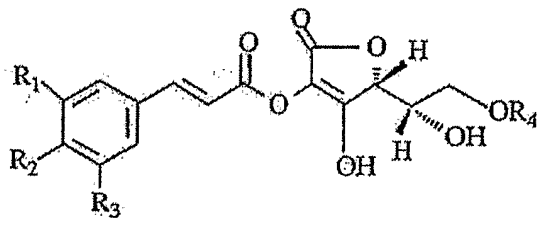
stimulate NO production, and BiDiL® which combines isosorbide dinitrate (NO donor) and hydralazine (antioxidant and vasodilator).

NOS stimulators

As examples of "NOS synthesis and/or activity stimulators", mention may, for example, be made of arachidonic acid, bradykinin, L-glutamic acid, histamine, hydroxyguanidine, interleukin 1-α, interleukin 1-β, interleukin-2, lipopolysaccharides, tetrahydro-L-biopterin and TNF-α.

Mention may also be made of L-2-pyrrolidone-5-carboxylic acid and its derivatives, as described in application EP 1 226 822.

Mention may also be made of the derivatives of mono- or diesters of cinnamic acid or of one of its derivatives and of vitamin C, such as the compounds of formula I

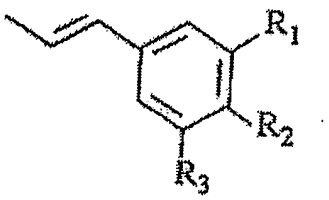


(I)

in which:

R_1, R_2 and R_3, independently of one another, represent H, or an OH, alkoxy, fluoroalkoxy or alkylcarbonyloxy radical, and

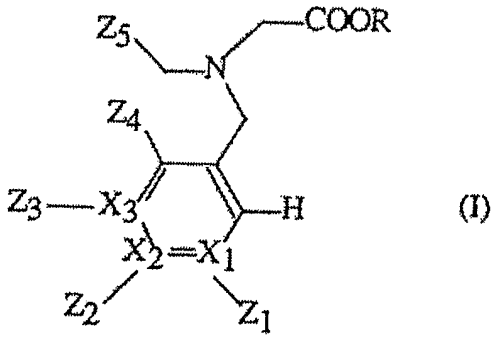
R_4 represents H or $-COR_5$, R_5 representing a C_1 to C_{20} linear or branched alkyl radical or the radical of formula:



and also the related substances or the substances that can generate them, and the analogues and precursors thereof.

Such compounds are described in greater detail in application EP 1 442 739, the content of which is incorporated into the present application by way of reference.

Mention may also be made of the compounds of formula I



(I)

in which:

Z_1, Z_2 and Z_3, independently of one another, represent NO_2, COOH, CF_3, a halogen atom or a group R_1, OR_1, SR_1 or NR_1R_2,

Z_4 represents H or a group R_1;

where R, R_1 and R_2, independently of one another, represent H or a C_1 to C_8 linear or branched alkyl group,

X_1, X_2 and X_3 represent: -C= or -N=, on the condition *

that

if X_1=N, then X_2=X_3=C and there is no substituent Z_1 on X_1,

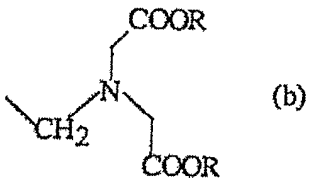
if X_2=N, then X_1=X_3=C and there is no substituent Z_2 on X_2,

if X_3=N, then X_2=X_1=C and there is no substituent Z_3 on X_3, i.e. it is a benzene or pyridine ring;

Z_5 represents:

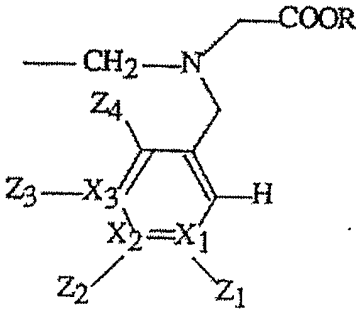
the group -COOR (a)

or the group:



(b)

or the group:



(c)

in which Z_1, Z_2, Z_3, X_1, X_2, X_3, R, R_1 and R_2 have the same meanings as above.

The compound may in particular be chosen from N-arylmethylene ethylenediaminetriacetates, N-aryl-

methyleneiminodiacetates or the N,N'-diarylmethylene ethylenediamineacetates as described in application EP 1 442 740, the content of which is incorporated into the present application by way of reference.

Preferably, use will be made of an NO donor or an NO releaser chosen from nitroglycerine (or trinitrine), S-nitroso-N-acetylpenicillamine (SNAP), diethylenetriamine nonoate (DETA NONOate), S-nitrosothiols and SNAGs (nitrosated thiosugars), sinitrodil, N,N-dimethylhexanediamine (DHMD/NO), isosorbide dinitrate (ISDN), isosorbide 5-mononitrate (IS5N), cyclosine, N-nitratopivaloyl-S-(N'-acetylalanyl)cysteine ethyl ester (SPM-5185) and arginine oligomers comprising from 1 to 5 units.

Antihypertensive agents

As examples, mention may be made of thiazides; angiotensin receptor inhibitors, such as losartan or candesartan; prostaglandins, particularly type E, and prostacyclins; ACE inhibitors, such as captopril or ramipril; potassium channel openers, such as minoxidil, chromakalim, diazoxide, nicorandil, pinacidil and derivatives; calcium channel blockers, such as nifedipine, verapamil, diltiazem, amlodipine; adrenergic receptor blockers, such as niacin (nicotinic acid), prazosine, hydralazine; muscarinic acetylcholine receptor activators.

As calcium channel blockers, mention may, for

example, be made of:

- agents that are active on the plasma membrane, that complex calcium and/or that are inhibitors of calcium entry, such as phenylalkylamines, for instance verapamil, anipamil, gallopamil, devapamil, falipamil, tiapamil, dihydropyridines, for instance nifedipine, amlodipine, dazodipine, felodipine, isradipine, lanicardipine, nimodipine, nisoldipine, nitrendipine, ryosidine, benzothiazepines, for instance diltiazem, diphenylpiperazines, for instance cinnarizine, flunarizine; or

- agents that are active within the cell and are involved in the release of intracellular calcium stores or in the inhibition of the formation of the calcium/calmodulin complex. These are, for example, agents that are involved at the level of the sarcoplasmic reticulum, for instance dantrolene and TMB-8, calmodulin antagonists, for instance phenothiazine, trifluoperazine, chlorpromazine or naphthalene derivatives, or local anaesthetics such as dibucaine or dopamine antagonists such as pimozide, haloperidol or calmidazolium.

Mention may also be made of manganese and/or salts that block calcium penetration into the cytoplasm in many cells.

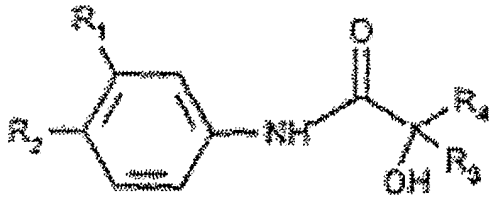
As organic salts of manganese, mention may be made of manganese gluconate or manganese carbonate or

manganese acetate or manganese citrate or manganese oleate or manganese oxalate.

As inorganic salts of manganese, mention may be made of the mineral salts such as manganese chloride or manganese borate or manganese nitrate or manganese phosphate or manganese sulphate.

Preferably, use will be made of potassium channel openers, among which mention may be made of:

- ATP-dependent potassium channel openers, such as minoxidil, cromakalim, diazoxide, nicorandil, pinacidil or 2-cyano-1-(4-pyridyl)-3-(1,2,2-trimethylpropyl)guanidine of the family of the cyanoguanidines and derivatives thereof;
- derivatives of benzopyran, of benzothiadiazine, of butanoic acid, of pyrimidine or of pyridine;
- the compounds described in application EP 0 886 515 corresponding to general formula (I)



(I)

in which

R1 is a cyano group, a halogen atom or an alkyl group having from 1 to 4 carbon atoms, substituted with at least one halogen atom;

R2 is a cyano group or a halogen atom;

R3 is an alkyl group having 1 or 2 carbon atoms, optionally substituted with at least one halogen atom;

R4 is a hydrogen atom or an alkyl group having from 1 to 4 carbon atoms, substituted with at least one halogen atom, or an aryl group, optionally substituted with one or more halogen atoms, or with one or more hydroxyl, carboxylic, nitro or cyano groups, linear or branched alkyl groups having 1 to 4 carbon atoms, linear or branched alkoxy groups having 1 to 4 carbon atoms, linear or branched alkanoyl groups having 1 to 4 carbon atoms, or perfluoroalkyl groups;

derivatives thereof and/or salts thereof.

As derivatives, use may, for example, be made of the compounds described in applications EP 0 915 857 and EP 0 916 652.

Phosphodiesterase inhibitors

As examples, mention may be made of type V phosphodiesterase inhibitors, such as visnadine and esculoside, icarine and its derivatives or extracts containing same, as described in application WO 2005/004858.

Flavonoids and flavoglycosides

As examples, mention may be made of Ginkgo

flavoglycosides, amentflavone or dimeric flavones of Gingko biloba in free form or in a form complexed with phospholipids, as described in application WO 2005/004858; hesperidin, alpha-G-hesperidin, hesperidin methyl chalcone, rutosides (for example, beta-hydroxyethyl rutoside, trimethyl rutoside).

Glucosides

Mention may in particular be made of escin, escin beta-sitosterol, adenosine or ATP (adenosine triphosphate); esculoside, hesperidin, alpha-G-hesperidin, rutosides (for example: beta-hydroxyethyl rutoside, trimethyl rutoside).

Plant extracts

Mention may, for example, be made of extract of everlast from Corsica (Helichrysum italicum) as described in particular in application WO 03/018730; extracts of blackcurrant (Ribes nigrum), of mistletoe, of barrenwort (Epimedium grandiflora), of kiwi (Actinidia chinensis L.), of cypress (Cupressus sempervirens), of melilot (Melissa officinalis), of lesser periwinkle (Vinca minora), of Centella asiatica, of Terminalia sericea (sericoside), extracts of calendulae, extracts of arnica, extracts of Ammi visnaga.

Vasodilator peptides (that are not NO donors):

Mention may be made of CGRP (calcitonin gene-related peptide), substance P (a decapeptide released

by a nerve ending) or VIP (vasoactive intestinal polypeptide) as described in application EP 225 639, the content of which is incorporated into the present application by way of reference.

Other vasodilators:

Mention may, for example, be made of nicotinic acid (niacin) and its derivatives, such as nicotinic acid esters, for example, xanthinol nicotinate, inositol nicotinate; salicylic acid and its esters; dihydroergotoxin methanesulphonate; dihydroergocornine methanesulphonate, dihydroergocristine methanesulphonate, cinnarizine, vincamine, pentoxyfyline, bamethane sulphate, bencyclane hydrogen fumarate, beta-pyridylcarbinol.

Temperature modulators

As other means of activating microcirculation in the skin, it is also possible to modulate the temperature using agents and/or formulations with a thermal (heating or cooling) effect.

Menthol or plant extracts and/or essential oils of menthol, of aloe vera or of ginseng are, for example, known as compounds with a freshening effect.

Camphor, or plant extracts or essential oils of eucalyptus or of ginger, are, for example, known as examples of compounds with a heating effect.

These compounds are generally used at concentrations ranging from 0.1% to 10% of the total

weight of the composition.

Agents for promoting the stimulation and/or maintenance of angiogenesis

Mention may in particular be made of:

- extracellular matrix-remodelling proteases, which facilitate vessel growth, such as collagenases or MMPs (matrix metalloproteinases), for instance MMP-1 or interstitial collagenase; MMP-8 or neutrophile collagenase, MMP-13 or collagenase 3, gelatinases (for example MMP-2, MMP-9), stromelysins (MMP-3);
- growth factors such as VEGF (vascular endothelial growth factor), PDGF (platelet derived growth factor); b-FGF (b-fibroblast growth factor); TGF-b (transforming growth factor TGF-b);
- leptin and lipolytic hormones. Some hormones, such as adrenocorticotropin, melanocyte-stimulating hormone, luteotropic hormone and glucagon, cause a vasodilation-related mobilization of free fatty acids. The vasodilation may originate from substances released during lipolysis.

Agents for promoting the stimulation of endothelial cell proliferation

Mention may in particular be made of:

- nitric oxide (NO) donors or precursors,
- nonpolymeric NO releasers,
- NO synthase (NOS) synthesis and/or activity stimulators.

Examples of such compounds are mentioned above.

Agents for promoting endothelial cell migration

Mention may in particular be made of elastin-derived and angiotensin II-derived peptides.

For an effect on the volume of the lips, and advantageously on the volume and the coloration of the lips, use will preferably be made of an agent chosen from nitric oxide (NO donors or precursors; nonpolymeric NO releasers; NO synthase synthesis and/or activity stimulators; potassium channel openers; calcium channel blockers; phosphodiesterase inhibitors; flavonoids; vasodilator peptides that are not NO donors; temperature modulators; agents for promoting the stimulation and/or maintenance of angiogenesis; agents for promoting the stimulation of endothelial cell proliferation; agents for promoting endothelial cell migration.

For an effect on the coloration of the lips, use will preferably be made of an agent chosen from nitric oxide NO donors or precursors with the exception of pyrimidine NO compounds; nonpolymeric NO releasers; NO synthase synthesis and/or activity stimulators;

antihypertensive agents, in particular potassium channel openers; phosphodiesterase inhibitors; flavonoids or glucosides, with the exception of hesperidin; plant extracts; vasodilator peptides that are not NO donors; temperature modulators; agents for promoting the stimulation and/or maintenance of angiogenesis; agents for promoting the stimulation of endothelial cell proliferation; agents for promoting endothelial cell migration.

Preferably, said agent will be chosen from an NO donor or precursor, a nonpolymeric NO releaser, an NOS synthesis and/or activity stimulator, a potassium channel opener, and mixtures thereof.

The NO donor or precursor will preferably be chosen from organic compounds comprising a nitro ($-NO_2$) or nitroso (-NO) substituent, oximes, heterocyclic NO donors, compounds that give nitroxyl, hydroxylamine, nonoate compounds ($-N(NO)O^-$), *N*-hydroxyguanidine and its salts (hemisulphate HG, or acetate NOHA), inorganic NO donors, transition metals-nitrosyl, nitrosodiphenylamine derivatives, cyclosine, N-nitrato-pivaloyl-S-(N'acetylalanyl)cysteine ethyl ester, photolabile NO donors, guanylate cyclase activators and/or cGMP stimulators.

The nonpolymeric NO releaser will preferably be chosen from peptides comprising from 1 to 5 amino acids chosen from L-arginine, histidine, lysine,

ornithine, glutamic acid, aspartic acid, serine, glycine, cysteine, threonine, and mixtures thereof.

Potassium channel opener will preferably be chosen from minoxidil, cromakalim, diazoxide, nicorandil, pinacidil, and derivatives of benzopyran, of benzothiadiazine, of butenoic acid, of pyrimidine or of pyridine.

Advantageously, said agent used according to the invention may be incorporated into a system that allows its release at the lips, after application of the composition thereto.

In particular, said agent may be adsorbed or incorporated into particulate structures having a size that may range from 1 mm to a few μm (10 μm), such as, for example, microcapsules, microparticles, vesicular dispersions of ionic type (liposomes or oleosomes) and/or nonionic type (niosomes) and/or dispersions of nanospheres. These particles may be advantageously porous and may consist of silicates or of aluminosilicates.

Examples of such formulations are described in particular in patents EP 199636, EP 375520, EP 447318, EP 557489, WO 97/12602, EP 1 151 741 or US 5 914 126.

By way of example, the microspheres may be prepared according to the method described in patent application EP 0 375 520.

The nanospheres may be in the form of an aqueous suspension and may be prepared according to the methods described in patent applications FR 0015686 and FR 0101438.

The oleosomes consist of an oil-in-water emulsion formed by oily globules provided with a lamellar liquid crystal coating dispersed in an aqueous phase (see patent applications EP 0 641 557 and EP 0 705 593).

The agent according to the invention may also be encapsulated in nanocapsules consisting of a lamellar coating obtained from a silicone surfactant as described in patent application EP 0 780 115; the nanocapsules may also be prepared from water-dispersible sulphonic polyesters according, for example, to the technique described in patent application FR 0113337.

The agent is present in the composition in an effective amount for obtaining the desired effect, i.e. the effect of making the lips full again and/or the effect of natural coloration of the lips. This effect can be directly measured by simple visual observation or by comparative image analysis.

By way of example, said agent will be present in the composition in an amount ranging from 0.001 to 10% by weight relative to the total weight of the composition, preferably from 0.01 to 5%, and better

still from 0.01 to 2%, and even better still from 0.02 to 1% by weight, relative to the total weight of the composition.

The composition may also comprise at least one agent chosen from solvents, oils, waxes, pasty substances, gums, fillers, dyestuffs, cosmetic active agents, thickeners, surfactants, moisturizers, softeners, sequestering agents, fragrances, neutralizing agents, preserving agents, antioxidants, UV-screening agents, bactericides, trace elements, odour absorbers, and mixtures thereof. The amounts of these various agents are those conventionally used in the field under consideration, for example from 0.01 to 20% of the total weight of the composition.

The composition may be in any pharmaceutical form normally used for topical application, and in particular in anhydrous form, in the form of an oily or aqueous solution, of an oily or aqueous gel, of an oil-in-water or water-in-oil emulsion, of a multiple emulsion, or of a dispersion of oil in water by virtue of vesicles located at the oil/water interface.

The composition of the invention may be in the form of a liquid, of a solid or of a semi-solid, in particular of a product moulded in the form of a stick or of a dish, of a small stick, of a paste, or of a more or less fluid cream.

The composition of the invention can be

obtained according to the methods of preparation conventionally used in cosmetics.

The term "physiologically acceptable medium" denotes a medium that is compatible with the lips of human beings.

The physiologically acceptable medium will be suited to the nature of the support to which the composition must be applied and also to the form in which the composition is intended to be packaged, in particular solid or fluid at ambient temperature and atmospheric pressure.

The composition according to the invention may comprise an aqueous cosmetic medium and/or a fatty phase.

The composition may comprise water or a mixture of water and hydrophilic organic solvents such as alcohols, and in particular linear or branched lower monoalcohols having from 2 to 5 carbon atoms, such as ethanol, isopropanol or n-propanol, polyols such as glycerol, diglycerol, propylene glycol, sorbitol, penthylene glycol, or polyethylene glycols. The hydrophilic phase may also contain hydrophilic C_2-C_4 aldehydes and C_2 ethers. The water or the mixture of water and hydrophilic organic solvents may be present in the composition according to the invention, or one of the base and/or surface compositions, at a content ranging from 0% to 90%, in particular 0.1% to 90%, by

weight, relative to the total weight of the composition, and preferably from 0% to 60% by weight (in particular 0.1% to 60% by weight).

The composition may also comprise a fatty phase, in particular consisting of fatty substances that are liquid at ambient temperature (in general 25°C) and/or of fatty substances that are solid at ambient temperature, such as waxes, pasty fatty substances, gums, and mixtures thereof. This fatty phase may also contain lipophilic organic solvents.

As fatty substances that are liquid at ambient temperature, often called oils, that can be used in the invention, mention may be made of: hydrocarbon-based plant oils such as liquid triglycerides of fatty acids having from 4 to 10 carbon atoms, for instance heptanoic or octanoic acid triglycerides, or else sunflower oil, corn oil, soya oil, grapeseed oil, sesame oil, apricot oil, macadamia oil, castor oil, avocado oil, caprylic/capric acid triglycerides, jojoba oil, shea butter oil; linear or branched hydrocarbons of mineral or synthetic origin, such as paraffin oils and derivatives thereof, petroleum jelly, polydecenes, hydrogenated polyisobutenes such as parleam; synthetic esters and ethers in particular of fatty acids such as, for example, Purcellin oil, isopropyl myristate, 2-ethylhexyl palmitate, 2-octyldodecyl stearate,

2-octyldodecyl erucate, isostearyl isostearate; hydroxylated esters such as isostearyl lactate, octyl hydroxystearate, octyldodecyl hydroxystearate, diisostearyl malate, triisocetyl citrate, fatty alcohol heptanoates, octanoates, decanoates; polyol esters such as propylene glycol dioctanoate, neopentyl glycol diheptanoate, diethylene glycol diisononanoate; and pentaerythritol esters; fatty alcohols having from 12 to 26 carbon atoms, such as octyldodecanol, 2-butyloctanol, 2-hexyldecanol, 2-undecylpentadecanol, oleyl alcohol; fluoro oils that are partially hydrocarbon-based and/or silicone-based; silicone oils such as volatile or nonvolatile polymethylsiloxanes (PDMSs) that are linear or cyclic, and liquid or pasty at ambient temperature, such as cyclomethicones or dimethicones, optionally comprising a phenyl group, such as phenyl trimethicones, phenyltrimethylsiloxy-diphenylsiloxanes, diphenylmethyldimethyltrisiloxanes, diphenyl dimethicones, phenyl dimethicones, polymethylphenylsiloxanes; mixtures thereof.

These oils may be present at a content ranging from 0.01 to 90%, and better still from 0.1 to 85% by weight, relative to the total weight of the composition.

The composition of the invention may also advantageously comprise a fatty substance that is solid or pasty at ambient temperature, such as gums or waxes.

The waxes may be hydrocarbon-based, fluorinated and/or silicone-based and may be of plant, mineral, animal and/or synthetic origin. In particular, the waxes may have a melting temperature of greater than 25°C, and better still greater than 45°C.

As waxes that can be used in the composition of the invention, mention may be made of beeswax, carnauba wax or candelilla wax, paraffin, microcrystalline waxes, ceresine or ozokerite; synthetic waxes such as polyethylene waxes or Fischer Tropsch waxes, silicone waxes such as alkyl or alkoxy dimethicones having from 16 to 45 carbon atoms.

The gums that may be used are generally high molecular weight polydimethylsiloxanes (PDMSs) or cellulose gums or polysaccharides, and the pasty substances are generally hydrocarbon-based compounds such as lanolins and derivatives thereof, alternatively PDMSs.

The term "pasty substance" is intended to mean a lipophilic fatty compound, with a reversible solid/liquid change in stage, which comprises a liquid fraction and a solid fraction at a temperature of 23°C. The term "pasty substance" is also intended to mean poly(vinyl laurate).

The pasty compounds are advantageously chosen from:

- lanolin and its derivatives,

- polymeric or nonpolymeric fluorinated compounds,
- polymeric or nonpolymeric silicone compounds,
- vinyl polymers, in particular:
    - olefin homopolymers,
    - olefin copolymers,
    - hydrogenated diene homopolymers and copolymers,
    - linear or branched oligomers which are homo- or copolymers of alkyl (meth)acrylates preferably having a C_8-C_{30} alkyl group,
    - oligomers which are homo- or copolymers of vinyl esters having C_8-C_{30} alkyl groups,
    - oligomers which are homo- and copolymers of vinyl ethers having C_8-C_{30} alkyl groups,
    - liposoluble polyethers resulting from polyetherification between one or more C_2-C_{100} diols, preferably C_2-C_{50} diols,
    - esters,
    - and mixtures thereof.

Among the liposoluble polyethers, preference is given in particular to copolymers of ethylene oxide and/or propylene oxide with alkylene oxides possessing a long C_6-C_{30} chain, more preferably such that the ratio by weight of the ethylene oxide and/or propylene oxide to alkylene oxides in the copolymer is from 5:95 to 70:30. In this family, mention will in particular be made of the copolymers such that the long-chain alkylene oxides are arranged in blocks having an

average molecular weight of from 1000 to 10 000, for example a polyoxyethylene/polydodecyl glycol block copolymer, such as the ethers of dodecanediol (22 mol) and of polyethylene glycol (45 EO) sold under the tradename Elfacos ST9 by Akzo Nobel.

Among pasty esters, preference is given in particular to:

- esters of an oligomeric glycerol, especially esters of diglycerol, in particular condensates of adipic acid and of glycerol, for which a portion of the hydroxyl groups of the glycerols have reacted with a mixture of fatty acids, such as stearic acid, capric acid, stearic acid and isostearic acid and 12-hydroxystearic acid, such as in particular those sold under the trade name Softisan 649 by the company Sasol,
- arachidyl propionate, sold under the trade name Waxenol 801 by Alzo,
- phytosterol esters,
- noncrosslinked polyesters resulting from the polycondensation between a linear or branched C_4-C_{50} di- or polycarboxylic acid and a C_2-C_{50} diol or polyol, other than the polyester described above,
- ester aliphatic esters resulting from the esterification of an aliphatic hydroxycarboxylic acid ester with an aliphatic monocarboxylic acid; and

mixtures thereof, such as

- the ester resulting from the esterification reaction of hydrogenated castor oil with isostearic acid in the proportions of 1 to 1 (1/1) or hydrogenated castor oil monoisostearate,
- the ester resulting from the esterification reaction of hydrogenated castor oil with isostearic acid in the proportions of 1 to 2 (1/2) or hydrogenated castor oil diisostearate,
- the ester resulting from the esterification reaction of hydrogenated castor oil with isostearic acid in the proportions of 1 to 3 (1/3) or hydrogenated castor oil triisostearate,
- and mixtures thereof.

Among pasty compounds of plant origin, a mixture of soybean sterols and of oxyethylenated (5 EO) oxypropylenated (5 PO) pentaerythritol sold under the reference Lanolide by the company Vevy will preferably be chosen.

The pasty compound preferably represents 1 to 99%, better still 1 to 60%, better still 2 to 30%, and even better still 5 to 15%, by weight of the composition.

The nature and the amount of the solid substances depend on the mechanical properties and the

textures desired. The composition may contain from 0 to 50% by weight of waxes, relative to the total weight of the composition, and better still from 1 to 30% by weight.

The term "fillers" should be understood to mean colourless or white, mineral or synthetic particles of any form, which are insoluble in the medium of the composition irrespective of the temperature at which the composition is manufactured. These fillers serve in particular to modify the rheology or the texture of the composition.

The fillers may be mineral or organic and of any form, platelet-shaped, spherical or oblong, irrespective of the crystallographic form (for example, lamellar, cubic, hexagonal, orthorhombic, etc.). Mention may be made of talc, mica, silica, kaolin, polyamide powder (Nylon®) (Orgasol® from Atochem), poly-β-alanine powder and polyethylene powder, tetrafluoroethylene polymer powders (Teflon®), lauroyllysine, starch, boron nitride, hollow polymeric microspheres such as those made of polyvinylidene chloride/acrylonitrile, for instance Expancel® (Nobel Industrie), or of acrylic acid copolymers (Polytrap® 603 from the company Dow Corning) and silicone resin microbeads (for example Tospearls® from Toshiba), elastomeric polyorganosiloxane particles, precipitated calcium carbonate, magnesium carbonate, magnesium

hydrocarbonate, hydroxyapatite, hollow silica microspheres (Silica Beads® from Maprecos), glass or ceramic microcapsules, metal soaps derived from organic carboxylic acids having from 8 to 22 carbon atoms, preferably from 12 to 18 carbon atoms, for example zinc stearate, magnesium stearate or lithium stearate, zinc laurate or magnesium myristate, Polypore® L 200 (Chemdal Corporation). Mention may also be made of silica-based fillers such as Aerosil 200 or Aerosil 300; Sunsphere L-31, Sunsphere H-31 sold by Asahi Glass; Chemicelen sold by Asahi Chemical; composites of silica and of titanium dioxide, such as the TSG series sold by Nippon Sheet Glass. Finally, mention may be made of polyurethane powders, in particular crosslinked polyurethane powders comprising a copolymer, said copolymer comprising trimethylol hexyllactone. In particular, it may be a hexamethylene diisocyanate/trimethylol hexyllactone polymer. Such particles are in particular available commercially, for example under the trade name Plastic Powder D-400® or Plastic Powder D-800® from the company Toshiki.

The content of fillers may range from 0.01% to 50% by weight, preferably ranging from 0.01% to 30% by weight, relative to the total weight of the composition.

For the purpose of the present invention, the term "dyestuff" is intended to mean a compound capable

of producing an optical effect when it is formulated in sufficient amounts in a suitable cosmetic medium. The dyestuffs may be present, in the composition, at a content ranging from 0.01% to 50% by weight, relative to the total weight of the composition, preferably from 0.1% to 30% by weight.

The dyestuff may in particular be chosen from dyes, pigments, pearlescent agents, and mixtures thereof.

The dyes are preferably liposoluble dyes, although water-soluble dyes may be used. The liposoluble dyes are, for example, Sudan Red, D & C Red 17, D & C Green 6, β-carotene, soybean oil, Sudan Brown, D & C Yellow 11, D & C Violet 2, D & C Orange 5, quinoline yellow or annatto. They may represent from 0 to 20% of the weight of the composition, and better still from 0.1 to 6%. The water-soluble dyes are in particular beetroot juice or methylene blue, and can represent from 0.1 to 6% by weight of the composition (if present).

The pigments may be chosen from mineral pigments, organic pigments and composite pigments (i.e. pigments based on mineral and/or organic materials). The term "pigments" should be understood to mean mineral or synthetic particles of any form, which have an optical effect and which are insoluble in the medium of the composition irrespective of the temperature at

which the composition is manufactured.

The mineral pigments may be chosen from metal oxide pigments, mica coated with titanium dioxide, mica coated with bismuth oxychloride, titanium mica coated with iron oxide, titanium mica coated with ferric blue, titanium mica coated with chromium oxide, and mixtures thereof.

The metal oxide pigments are, for example, iron oxides, titanium dioxide, zinc oxides, zirconium oxides, cerium oxides, and mixtures thereof. The mineral pigments are preferably metal oxide pigments. The pigments may be present in the composition at a content ranging from 0.01% to 25% by weight, relative to the total weight of the composition, and preferably ranging from 1 to 12% by weight, and preferentially ranging from 3 to 8% by weight.

The organic pigments may be chosen from the pigments and lakes mentioned in the work "International Cosmetic Ingredient Dictionary and Handbook", edition 1997, page 371 to 386 and 524 to 528, published by "The Cosmetic, Toiletry and Fragrance Association", the content of which is incorporated into the present application by way of reference.

The pearlescent agents may be chosen, for example, from mica coated with titanium oxide, with iron oxide, with natural pigment or with bismuth oxychloride, such as coloured titanium mica.

The expression "hydrophilic or lipophilic cosmetic active agents" that can be used in the composition of the invention is intended to mean in particular active agents intended to embellish the appearance of the lips. This active agent may be chosen in particular from:

- agents for stimulating the synthesis of dermal or epidermal macromolecules and/or preventing degradation thereof (for example, synthesis of collagen, elastin, etc.),
- moisturizers,
- desquamating agents,
- propigmenting agents,
- anti-pollution agents or free radical scavengers,
- calmatives,
- cicatrizing agents,
- tensioning agents.

Agents for stimulating the synthesis of macromolecules

The cells of the dermis, in particular the fibroblasts, produce collagen, elastin and glycoprotein molecules. These molecules confer the volume and the density to the lips and their outline, and also their firmness. With the effect of age or else under the effect of UV rays, a notable decrease in these molecules occurs, along with degradation of collagen and elastin fibres due to the effect of collagenase or of elastase. This degradation or decrease in the

production of these molecules induces a loss of firmness of the lips and of their outline, causing in particular the appearance of wrinkles.

Among the active agents for stimulating the macromolecules of the dermis or preventing degradation thereof, mention may be made of those that act:

- either on the synthesis of collagen, such as extracts of Centella asiatica; asiaticosides and derivatives; ascorbic acid or vitamin C and its derivatives, such as its salts or its esters, in particular 5,6-di-O-dimethylsilyl ascorbate (sold by the company Exsymol under the reference PRO-AA), the potassium salt of dl-alpha-tocopheryl-dl-ascorbyl phosphate (sold by the company Senju Pharmaceutical under the reference Sepivital EPC), ascorbyl magnesium phosphate, ascorbyl sodium phosphate (sold by the company Roche under the reference Stay-C 50) and ascorbyl glucoside (sold by the company Hayashibara); synthetic peptides, such as iamin, biopeptide CL or palmitoyloligopeptide sold by the company Sederma; peptides extracted from plants, such as the soybean hydrolysate sold by the company Coletica under the trade name Phytokine®; plant hormones, such as auxins and lignans; the palmitoyl of lysine-threonine-lysine-serine pentapeptide sold in particular under the name "Matrixyl" by the company Sederma; dimethylaminoethanol; extracts of Bupleurum chinensis rhizome, such as those sold under the names

"Pleurimincyl" or "Lipocare" by the company Sederma; acylated hydrolysates of wheat protein, in particular acylated with a palmitoyl group, such as that sold under the name "Lipacid PVB" by the company Seppic; creatine; coenzyme Q10;

- or on the synthesis of elastin, such as the extract of Saccharomyces cerivisiae sold by the company LSN under the trade name Cytovitin®; and the extract of the alga Macrocystis pyrifera sold by the company Secma under the trade name Kelpadelie®; melibiose; soybean proteins;

- or on the synthesis of glycosaminoglycans, such as the product of fermentation of milk by lactobacillus vulgaris, sold by the company Brooks under the trade name Biomin yogourth®; the extract of the brown alga Padina pavonica sold by the company Alban Müller under the trade name HSP3®; and the extract of Saccharomyces cerevisiae available in particular from the company Silab under the trade name Firmalift® or from the company LSN under the trade name Cytovitin®;

- or on the synthesis of fibronectin, such as the extract of the zooplankton Salina sold by the company Seporga under the trade name GP4G®; the yeast extract available in particular from the company Alban Müller under the trade name Drieline®; and the palmitoyl pentapeptide sold by the company Sederma under the trade name Matrixil®;

- or on the inhibition of metalloproteinases (matrix metalloproteinases or MMPs) such as more particularly MMP 1, 2, 3 or 9. Mention may be made of: retinoids and derivatives, oligopeptides and lipopeptides, lipoamino acids, the malt extract sold by the company Coletica under the trade name Collalift®; extracts of blueberry or of rosemary; lycopene; isoflavones, their derivatives or the plant extracts containing them, in particular extracts of soybean sold, for example, by the company Ichimaru Pharcos under the trade name Flavosterone SB®), of red clover, of flax, of kakkon or of sage;

- or on the inhibition of serine proteases, such as leukocyte elastase or cathepsin G. Mention may be made of: the peptide extract of leguminous plant (Pisum sativum) seeds, sold by the company LSN under the trade name Parelastyl®; heparinoids; and pseudodipeptides, such as {2-[acetyl-(3-trifluoromethylphenyl)amino]-3-methylbutyrylamino}acetic acid.

Among the active agents for stimulating fillagrin and keratins, mention may in particular be made of the extract of lupin sold by the company Silab under the trade name Structurine®; the extract of Fagus sylvatica beech buds sold by the company Gattefosse under the trade name Gatuline®; and the extract of the zooplankton Salina sold by the company Seporga under the trade name GP4G®.

Preferably, the agents for stimulating the synthesis of dermal or epidermal macromolecules and/or preventing degradation thereof are chosen from extracts of Centella asiatica, ascorbic acid and its derivatives, peptides extracted from plants, such as the soybean hydrolysates sold by the company Coletica under the trade name Phytokine®, or the extract of Saccharomyces cerivisiae sold by the company LSN under the trade name Cytovitin®; the extract of the brown alga Padina pavonica sold by the company Alban Müller under the trade name HSP3®; retinoids and derivatives; extracts of rosemary; the peptide extracts of leguminous plant (Pisum sativum) seeds sold by the company LSN under the trade name Parelastyl®; {2-[acetyl-(3-trifluoromethylphenyl)amino]-3-methylbutyrylamino}acetic acid; extract of lupin; and mixtures thereof.

Moisturizers

The term "moisturizer" is intended to mean:

- either a compound acting on the barrier function, for the purpose of keeping the stratum corneum moisturized, or an occlusive compound. Mention may be made of ceramides, sphingoid-based compounds, lecithins, glycosphingolipids, phospholipids, cholesterol and its derivatives, phytosterols (stigmasterol, β-sitosterol, campesterol), essential fatty acids, 1,2-diacylglycerol, 4-chromanone, pentacyclic triterpenes

such as ursolic acid, petroleum jelly and lanolin;
- or a compound that directly increases the water content of the stratum corneum, such as threalose and its derivatives, hyaluronic acid and its derivatives, glycerol, pentanediol, sodium pidolate, serine, xylitol, sodium lactate, polyglyceryl acrylate, ectoin and its derivatives, chitosan, oligosaccharides and polysaccharides, such as the product sold under the reference Pentavitin, honey, alginates (in particular the product Sobalg PH 154 sold by the company Grindsted), cyclic carbonates, N-lauroylpyrrolidone-carboxylic acid and its salts, in particular the sodium salt sold under the reference Nalidone, and N-α-benzoyl-L-arginine;
- or a compound that activates the sebaceous glands, such as steroid derivatives (including DHEA, its 7-oxidized and/or 17-alkylated derivatives, and sapogenins), methyl dihydrojasmonate, and vitamin D and its derivatives.

These compounds may represent from 0.001% to 30%, and preferably from 0.01 to 20%, of the total weight of the composition according to the invention.

Desquamating agents

The term "desquamating agent" is intended 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 acid, citric acid, lactic acid, tartaric acid, malic acid or mandelic acid; urea; gentisic acid; oligofucoses; cinnamic acid; extract of Saphora japonica; resveratrol and certain jasmonic acid derivatives;

- or on the enzymes involved in desquamation or degradation of corneodesmosomes, such as glycosidases, stratum corneum chymotryptic enzyme (SCCE), or even other proteases (trypsin, chymotrypsin-like). Mention may be made of agents for chelating mineral salts: EDTA; N-acyl-N,N',N'-ethylenediaminetriacetic acid; aminosulphonic compounds, and in particular (N-2-hydroxyethylpiperazine-N-2-ethane)sulphonic acid (HEPES); 2-oxothiazolidine-4-carboxylic acid (procysteine) derivatives; derivatives of alpha-amino acids of the glycine type (as described in EP 0 852 949, and also the sodium methylglycinediacetate sold by BASF under the trade name Trilon M); honey; sugar derivatives such as O-octanoyl-6-D-maltose and N-acetylglucosamine.

Propigmenting agents

As propigmenting agent, mention may be made of the extract of burnet (Sanguisorba officinalis) sold by the company Maruzen, and extracts of chrysanthemum (Chrysanthemum morifolium).

Anti-pollution agent or free-radical scavenger

The term "anti-pollution agent" is intended to mean any compound capable of trapping ozone, monocyclic or polycyclic aromatic compounds such as benzopyrene and/or heavy metals such as cobalt, mercury, cadmium and/or nickel. The term "free-radical scavenger" is intended to mean any compound capable of trapping free radicals.

As ozone-trapping agents that may be used in the composition according to the invention, mention may in particular be made of vitamin C and its derivatives, including ascorbyl glucoside; phenols and polyphenols, in particular tannins, ellagic acid and tannic acid; epigallocatechin and natural extracts containing it; extracts of olive tree leaf; extracts of tea, in particular of green tea; anthocyans; extracts of rosemary; phenol acids, in particular chlorogenic acid; stilbenes, in particular resveratrol; sulphur-containing amino acid derivatives, in particular S-carboxymethylcysteine; ergothioneine; N-acetylcysteine; chelating agents, for instance N,N'-bis(3,4,5-trimethoxybenzyl)ethylenediamine or one of its salts, metal complexes or esters; carotenoids such as crocetin; various starting materials, for instance the mixture of arginine, histidine ribonucleate, mannitol, adenosine triphosphate, pyridoxine, phenylalanine, tyrosine and hydrolyzed RNA, sold by the

company Laboratoires Sérobiologiques under the trade name CPP LS 2633-12F®, the water-soluble fraction of corn sold by the company Solabia under the trade name Phytovityl®, the mixture of extract of fumetory and of extract of lemon sold under the trade name Unicotrozon C-49® by the company Induchem, and the mixture of extracts of ginseng, of apple, of peach, of wheat and of barley, sold by the company Provital under the trade name Pronalen Bioprotect®.

As agents for trapping monocyclic or polycyclic aromatic compounds, that may be used in the composition according to the invention, mention may in particular be made of tannins such as ellagic acid; indole derivatives, in particular 3-indolecarbinol; extracts of tea, in particular of green tea, extracts of water hyacinths or Eichornia crassipes; and the water-soluble fraction of corn sold by the company Solabia under the trade name Phytovityl®.

Finally, as heavy-metal-trapping agents that may be used in the composition according to the invention, mention may in particular be made of chelating agents such as EDTA, the pentasodium salt of ethylenediaminetetramethylenephosphonic acid, and N,N'-bis(3,4,5-trimethoxybenzyl)ethylenediamine or one of its salts, metal complexes or esters; phytic acid; chitosan derivatives; extracts of tea, in particular of green tea; tannins such as ellagic acid; sulphur-

containing amino acids such as cysteine; extracts of water hyacinth (Eichornia crassipes); and the water-soluble fraction of corn sold by the company Solabia under the trade name Phytovityl®.

The free-radical scavengers that may be used in the composition according to the invention comprise, besides certain anti-pollution agents mentioned above, vitamin E and its derivatives, such as tocopheryl acetate; bioflavonoids; coenzyme Q10 or ubiquinone; certain enzymes, such as catalase, superoxide dismutase and extracts of wheatgerm containing same, lactoperoxidase, glutathione peroxidase and quinone reductases; glutathione; benzylidenecamphor; benzylcyclanones; substituted naphthalinones; pidolates; phytanetriol; gamma-oryzanol; guanosine; lignins; and melatonin.

Calmatives

As calmatives that may be used in the composition according to the invention, mention may be made of: pentacyclic triterpenes and extracts of plants (e.g.: Glycyrrhiza glabra) containing them, such as β-glycyrrhetinic acid and salts and/or derivatives thereof (glycyrrhetinic acid monoglucuronide, stearyl glycyrrhetinate or 3-stearoyloxyglycyrrhetic acid), ursolic acid and its salts, oleanolic acid and its salts, betulinic acid and its salts, extracts of plants such as *Paeonia suffruticosa* and/or *lactiflora*,

Laminaria saccharina, Boswellia serrata, Centipeda cunnighami, Helianthus annuus, Linum usitatissimum, Cola nitida, Epilobium Angustifolium, Aloe vera or *Bacopa monieri,* salicylic acid salts, and in particular zinc salicylate, canola oil, bisabolol and camomile extracts, allantoin, Sepivital EPC (phosphoric diester of vitamins E and C) from Seppic, omega-3 unsaturated oils such as musk rose oil, blackcurrant oil, ecchium oil or fish oil, plankton extracts, capryloylglycine, Seppicalm VG (sodium palmitoylproline and Nymphea alba) from Seppic, tocotrienols, piperonal, an extract of clove, phytosterols, cortisone, hydrocortisone, indomethacin and betamethasone.

Cicatrizing agents

Examples of cicatrizing agents are in particular the extract of fern leaves sold under the reference Mamaku Vital Essence by Lucas Meyer, and the rice peptides obtained by hydrolysis of rice proteins, sold under the name Nutripeptide by Silab.

Tensioning agents

Mention may in particular be made of:

(1) synthetic polymers, such as polyurethane latices or acrylic-silicone latices, in particular those described in patent application EP 1 038 519, such as a propylthio(polymethyl acrylate), propylthio(polymethyl methacrylate) and propylthio(polymethacrylic acid) grafted polydimethylsiloxane, or alternatively a

propylthio(polyisobutyl methacrylate) and propylthio(polymethacrylic acid) grafted polydimethylsiloxane. Such grafted silicone polymers are sold in particular by the company 3M under the trade names VS 80, VS 70 or LO21,

(2) polymers of natural origin, in particular (a) polyholosides, for example (i) in the form of starch derived in particular from rice, from corn, from potato, from cassava, from pea, from *Triticum aestivum* wheat, from oat, etc., or (ii) in the form of carrageenans, alginates, agars, gellans, cellulose-based polymers and pectins, advantageously as an aqueous dispersion of gel microparticles, and

(b) latices consisting of shellac resin, sandarac gum, dammar resins, elemi gums, copal resins, cellulose-based derivatives, and mixtures thereof,

(3) plant proteins and protein hydrolysates, in particular from corn, rye, *Triticum aestivum* wheat, buckwheat, sesame, spelt, pea, bean, lentil, soybean and lupin,

(3) mixed silicates, especially phyllosilicates, and in particular laponites,

(4) wax microparticles chosen, for example, from carnauba wax, candelilla wax or esparto grass wax,

(5) colloidal particles of inorganic filler having a number-average diameter of between 0.1 and 100 nm, preferably between 3 and 30 nm, and chosen, for example

from: silica, silica-alumina composites, cerium oxide, zirconium oxide, alumina, calcium carbonate, barium sulphate, calcium sulphate, zinc oxide and titanium dioxide.

The care and/or makeup composition for the lips may be in the form of a lipstick, of a liquid gloss, of a lipstick paste, a lipliner pencil, a lip balm, a lip varnish, otherwise called lip lacquer.

The lip balm will in particular be intended to protect the lips against the cold and/or the sun and/or the wind.

The liquid gloss, also called liquid lipstick or liquid sheen, is a fluid product intended to be applied to the lips and packaged, for example, in a container provided with an applicator, this applicator comprising a gripping member which also serves as cap for closing the container, and an applying element.

According to a particular embodiment of the invention, said agent with a natural effect that makes the lips full again and/or that stimulates the coloration of the lips, using the compositions of the invention, is combined with at least one makeup agent with an optical volume effect.

This makeup agent with an optical volume effect is intended to reinforce the volume effect obtained with the first agent and/or confer on the composition applied to the lips an immediate volumizing

optical effect passed on over time by the natural volumizing effect mediated by the first agent. The presence of the first agent in the composition also makes it possible to decrease the normally effective concentrations of the second agent so as to obtain the desired effect on the volume and/or the coloration of the lips, so as to promote the natural appearance of the makeup.

As a "makeup agent with an optical volume effect", use may, for example, be made of goniochromatic pigments, reflective particles, and mixtures thereof.

The term "goniochromatic pigment" is intended in particular to mean a pigment capable of producing various colours depending on the incidence of the light and the angle of observation.

Preferably, the goniochromatic pigments are goniochromatic pigments with a multilayer interference structure. In particular, use may be made of the goniochromatic pigments described in application EP 1 382 323.

The multilayer structure of the goniochromatic pigments may contain at least two layers, each layer, possibly independently of the other layer(s), being made of at least one material chosen from the group consisting of the following materials: MgF_2, CeF_3, ZnS, ZnSe, Si, SiO_2, Ge, Te, Fe_2O_3, Pt, Va,

Al_2O_3, MgO, Y_2O_3, S_2O_3, SiO, HfO_2, ZrO_2, CeO_2, Nb_2O_5, Ta_2O_5, TiO_2, Ag, Al, Au, Cr, Cu, Rb, Ti, Ta, W, Zn, MoS_2, cryolite, alloys and polymers, and combinations thereof.

By way of example, these pigments may be the pigments of silica/titanium oxide/tin oxide structure sold under the name Xirona Magic by the company Merck, the pigments of silica/brown iron oxide structure sold under the name Xirona Indian Summer by the company Merck and the pigments of silica/titanium oxide/mica/tin oxide structure sold under the name Xirona Caribbean Blue by the company Merck. Mention may also be made of Sicopearl Fantastico manufactured or sold by the company BASF, Colorstream manufactured or sold by the company Merck, Chromaflair manufactured or sold by the company Flex, Xirallic manufactured or sold by the company Merck; the Infinite Colors pigments from the company Shiseido.

By way of example of pigments with a polymeric multilayer structure, mention may be made of those sold by the company 3M under the name Color Glitter.

As liquid-crystal goniochromatic particles, use may, for example, be made of those sold by the company Chenix and also that sold under the name Helicone® HC by the company Wacker.

In general, the structure is composed of

alternating layers of low optical index and high optical index.

The goniochromatic pigments may be present in the composition according to the invention at a content ranging from 0.01% to 50% by weight, relative to the total weight of the composition, preferably from 0.1 to 30% by weight, and better still from 0.3% to 20% by weight.

The term "reflective particles" is intended in particular to mean particles whose size, structure and surface finish allow them to reflect incident light with sufficient intensity to be able to create, at the surface of the composition claimed, when the latter is applied to the support to be made up, highlight points visible to the naked eye, i.e. points that are more luminous and at contrast with their surroundings by appearing to shine. Mention may, for example, be made of particles containing a natural or synthetic substrate, at least partially coated with a layer of at least one metal, particles with a synthetic substrate at least partially coated with at least one layer of a metal compound, and in particular of a metal oxide, particles formed from stacking of at least two layers with different refractive indices, in particular two layers of polymers, and particles of metal oxides.

The metal may be chosen, for example, from Ag, Au, Cu, Al, Ni, Sn, Mg, Cr, Mo, Ti, Pt, Va, Rb, W,

Zn, Ge, Te and Se, and alloys thereof. Ag, Au, Al, Zn, Ni, Mo, Cr and Cu and alloys thereof (for example bronzes and brasses) are preferred metals.

By way of examples, use may be made of particles with a silver-coated glass substrate, in the form of platelets, sold under the name Microglass Metashine REFSX 2025 PS by the company Toyal; or particles with a nickel/chromium/molybdenum alloy-coated glass substrate, sold under the name Crystal Star GF 550, or GF 2525 by this same company.

The reflective particles, irrespective of their form, can also be chosen from particles with a synthetic substrate at least partially coated with at least one layer of at least one metal compound, in particular a metal oxide, chosen, for example, from titanium oxides, in particular TiO_2, iron oxides, in particular Fe_2O_3, tin oxides, chromium oxides, barium sulphate and the following compounds: MgF_2, CrF_3, ZnS, ZnSe, SiO_2, Al_2O_3, MgO, Y_2O_3, SeO_3, SiO, HfO_2, ZrO_2, CeO_2, Nb_2O_5, Ta_2O_5 and MoS_2, and mixtures or alloys thereof.

By way of example of such particles, mention may, for example, be made of particles containing a substrate of synthetic mica coated with titanium dioxide, or glass particles coated either with brown iron oxide, or with titanium oxide, with tin oxide or with a mixture thereof, such as those sold under the trade name Reflecks® by the company Engelhard.

Also suitable for the invention are the pigments of the Metashine 1080R range sold by the company Nippon Sheet Glass Co. Ltd. These pigments, more particularly described in patent application JP 2001-11340, are flakes of C-Glass comprising 65 to 72% of SiO_2, coated with a layer of rutile-type titanium oxide (TiO_2). These glass flakes have an average thickness of 1 micron and an average size of 80 microns, i.e. an average size/average thickness ratio of 80. They exhibit blue, green, yellow or silver-tinted glints depending on the thickness of the layer of TiO_2.

Mention may also be made of particles of between 80 and 100 μm in size, containing a synthetic mica substrate (fluorophlogopite) coated with titanium dioxide representing 12% of the total weight of the particle, sold under the name Prominence by the company Nihon Koken.

The reflective particles may be present in the composition by being dispersed homogeneously, for example at a content ranging from 0.1% to 20% relative to the total weight of the composition, preferably from 1% to 15% by weight, and better still from 1% to 10% by weight, for example approximately 2%, in particular for a composition to be applied to the lips.

The invention also relates to a cosmetic composition comprising, in a physiologically acceptable

medium, (i) at least one agent for promoting the production of NO in and/or on the lips, chosen from nitric oxide NO donors or precursors, with the exception of the pyrimidine NO compounds; nonpolymeric NO releasers; NO synthase synthesis and/or activity stimulators; or (ii) other agents for promoting microcirculation in the skin, chosen from potassium channel openers; agents for promoting the stimulation and/or maintenance of angiogenesis; agents for promoting the stimulation of endothelial cell proliferation; agents for promoting endothelial cell migration; and mixtures thereof; and characterized in that it is in the form of a lipstick, a liquid gloss, a lip paste, a lipliner pencil, a lip balm, or a lip varnish, otherwise named lip lacquer.

In particular, said agent (i) is chosen from nitroglycerine (or trinitrine), S-nitroso-N-acetylpenicillamine (SNAP), diethylenetriamine nonoate (DETA NONOate), S-nitrosothiols and SNAGs (nitrosated thiosugars), Sinitrodil, N,N-dimethylhexanediamine (DHMD/NO), isosorbide dinitrate (ISDN), isosorbide 5-mononitrate (IS5N), cyclosine, N-nitratopivaloyl-S-(N'-acetylalanyl)cysteine ethyl ester (SPM-5185) and oligomers of arginine comprising from 1 to 5 amino acids.

The potassium channel opener will preferentially be chosen from minoxidil, cromakalim,

diazoxide, nicorandil, pinacidil and derivatives of benzopyran, of benzothiadiazine, of butenoic acid, of pyrimidine or of pyridine.

Advantageously, said agent will be incorporated into a system that allows its release in the skin, after application of the composition thereto. In particular, said agent can be adsorbed onto or encapsulated in particulate structures having a size that can range from 1 nm to a few μm (10 μm), such as, for example, microcapsules, microparticles, vesicular dispersions of ionic (liposomes or oleosomes) and/or nonionic (niosomes) type and/or dispersions of nanospheres. These particles may be advantageously porous and may consist of silicates or of aluminosilicates.

Said agent will be present in the composition in an amount sufficient to obtain the desired effect, i.e. a volumizing effect on the lips or an effect making the lips full again and/or an effect on the natural coloration of the lips.

For example, this amount may range from 0.001 to 10% by weight, relative to the total weight of the composition, preferably from 0.01 to 5%, and better still from 0.01 to 2%, and even better still from 0.02 to 1% by weight, relative to the total weight of the composition.

The composition may be in any of the

pharmaceutical forms suitable for topical application to the lips, in particular a form among those described above in the description.

In one specific composition of the invention, said agent is combined with at least one makeup agent with an optical volume effect on the lips, preferably chosen from goniochromatic pigments, reflective particles and mixtures thereof, as described above.

Examples of such compounds are described above.

The composition may also comprise at least one agent chosen from fillers, dyestuffs, cosmetic active agents, thickeners, surfactants, moisturizers, softeners, sequestering agents, fragrances, neutralizing agents, preserving agents, antioxidants, UV-screening agents, bactericides, trace elements, and mixtures thereof.

Examples of such compounds are described above in the description.

The invention also relates to a process for making up and/or for caring for the lips, characterized in that a composition as defined above is applied to the lips.

In particular, the composition is applied to thin lips or women with thin lips.

The examples submitted below are presented by way of nonlimiting illustration of the invention.

EXAMPLES

Lip balm

- nitroglycerine (trinitrine)		0.25%
- carnauba wax		12.75%
- oxypropylenated lanolin wax (5 propylene oxides)		15.00%
- castor oil	qs	100%

After the carnauba wax and lanolin wax have been melted at 100°C, the castor oil containing acexamic acid is introduced and the entire combination is mixed and poured into an appropriate mould.

Lipstick

- polyethylene wax (MW 500)	12.00%
- liquid lanolin	15.00%
- phenyl trimethicone (DC 556 from Dow Corning)	63.34%
- pigments	8.66%
- minoxidil	1.00%

Preparation: The pigments and the minoxidil are milled in a mixture containing phenyl trimethicone and the liquid lanolin. The rest of the constituents are melted at 100°C and are then added to the mixture. After homogenization, the entire combination is poured into an appropriate mould. In this lipstick, the minoxidil is dispersed.

CLAIMS

1. Cosmetic use (i) of at least one agent for promoting the production of nitric oxide NO in and/or on the lips chosen from nitric oxide (NO) donors or precursors; nonpolymeric NO releasers; and NO synthase synthesis and/or activity stimulators; or (ii) of other agents for promoting microcirculation in the skin, chosen from potassium channel openers; calcium channel blockers; phosphodiesterase inhibitors; flavonoids; vasodilator peptides that are not NO donors; temperature modulators; agents for promoting the stimulation and/or maintenance of angiogenesis; agents for promoting the stimulation of endothelial cell proliferation; agents for promoting endothelial cell migration; and mixtures thereof, as a makeup and/or care composition for the lips, as an agent for naturally making the lips full again.

2. Use according to Claim 1, characterized in that said agent is intended to augment the size and/or the volume of the lips and/or to model them and/or to make them smoother.

3. Use according to Claim 2, characterized in that said agent is also intended to stimulate the naturally pinkish coloration of the lips.

4. Cosmetic use (i) of at least one agent for promoting the production of nitric oxide NO in

and/or on the lips, chosen from nitric oxide NO donors or precursors, with the exception of pyrimidine N-oxide compounds, nonpolymeric NO releasers, NO synthase synthesis and/or activity stimulators or (ii) of other agents for promoting microcirculation in the skin, chosen from antihypertensive agents; phosphodiesterase inhibitors; flavonoids or glucosides, with the exception of hesperidin; plant extracts; vasodilator peptides that are not NO donors; temperature modulators; agents for promoting the stimulation and/or maintenance of angiogenesis; agents for promoting the stimulation of endothelial cell proliferation; agents for promoting endothelial cell migration; and mixtures thereof, in a makeup and/or care composition for the lips, as an agent for stimulating the naturally pinkish coloration of the lips.

5. Use according to any one of Claims 1 to 4, characterized in that said agent for promoting the production of NO in and/or on the lips is chosen from organic compounds comprising a nitro ($-NO_2$) or nitroso (-NO) substituent, oximes, heterocyclic NO donors, compounds that give nitroxyl, hydroxylamine, nonoate compounds ($-N(NO)O^-$), *N*-hydroxyguanidine and its salts (hemisulphate HG, or acetate NOHA), inorganic NO donors, nitrosyl transition metals, nitrosodiphenylamine derivatives, cyclosine, N-nitrato-pivaloyl-S-(N'-acetylalanyl)cysteine ethyl ester,

photolabile NO donors, guanylate cyclase activators and/or cGMP stimulators, peptides comprising from 1 to 5 amino acids chosen from L-arginine, histidine, lysine, ornithine, glutamic acid, aspartic acid, serine, glycine, cysteine and threonine, and mixtures thereof.

6. Use according to any one of Claims 1 to 5, characterized in that said agent for promoting the production of nitric oxide NO in and/or on the lips is chosen from nitroglycerine, S-nitroso-N-acetylpenicillamine (SNAP), diethylenetriamine nonoate (DETA NONOate), S-nitrosothiols and SNAGs (nitrosated thiosugars), Sinitrodil, N,N-dimethylhexanediamine (DHMD/NO), isosorbide dinitrate (ISDN), isosorbide 5-mononitrate (IS5N), cyclosine, N-nitratopivaloyl-S-(N'-acetylalanyl)cysteine ethyl ester (SPM-5185) and arginine oligomers comprising from 1 to 5 amino acids.

7. Use according to any one of Claims 1 to 4, characterized in that said agent for promoting microcirculation in the skin is a potassium channel opener chosen from minoxidil, cromakalim, diazoxide, nicorandil, pinacidil, and derivatives of benzopyran, of benzothiadiazine, of butenoic acid, of pyrimidine or of pyridine.

8. Use according to any one of Claims 1 to 7, characterized in that said agent is present in the composition in an amount ranging from 0.001 to 10% by

weight relative to the total weight of the composition, preferably from 0.01 to 5%, and even more preferentially from 0.01 to 2% by weight relative to the total weight of the composition.

9. Use according to any one of Claims 1 to 8, characterized in that said agent is adsorbed or incorporated into particles having a size ranging from 1 nm to 10 μm.

10. Use according to any one of Claims 1 to 9, characterized in that the composition also comprises at least one agent chosen from solvents, oils, waxes, pasty substances, gums, fillers, dyestuffs, cosmetic active agents, thickeners, surfactants, moisturizers, softeners, sequestering agents, fragrances, neutralizing agents, preserving agents, antioxidants, UV-screening agents, bactericides, odour absorbers, trace elements, and mixtures thereof.

11. Use according to Claim 10, characterized in that the cosmetic active agents are chosen from agents for stimulating the synthesis of dermal or epidermal macromolecules and/or preventing degradation thereof, moisturizers, desquamating agents, propigmenting agents, anti-pollution agents or free-radical scavengers, calmatives, cicatrizing agents and tensioning agents.

12. Use according to any one of Claims 1 to 11, characterized in that said agent is combined, in

the composition, with at least one makeup agent with an optical volume effect on the lips, such as goniochromatic pigments, reflective particles and mixtures thereof.

13. Use according to any one of Claims 1 to 12, characterized in that the composition is in the form of a lipstick, a liquid gloss, a lip paste, a lipliner pencil, a lip balm or a lip varnish.

14. Cosmetic composition comprising, in a physiologically acceptable medium, (i) at least one agent for promoting the production of NO in and/or on the lips, chosen from NO donors or precursors, with the exception of pyrimidine NO compounds; nonpolymeric NO releasers; NO synthase synthesis and/or activity stimulators; or (ii) other agents for promoting microcirculation in the skin, chosen from potassium channel openers; agents for promoting the stimulation and/or maintenance of angiogenesis; agents for promoting the stimulation of endothelial cell proliferation; agents for promoting endothelial cell migration, and mixtures thereof, and characterized in that it is in the form of a lipstick, a liquid gloss, a lip paste, a lipliner pencil, a lip balm, or a lip varnish.

15. Composition according to Claim 14, characterized in that said agent (i) is chosen from nitroglycerine, S-nitroso-N-acetylpenicillamine (SNAP),

diethylenetriamine nonoate (DETA NONOate), S-nitrosothiols and SNAGs (nitrosated thiosugars), Sinitrodil, N,N-dimethylhexanediamine (DHMD/NO), isosorbide dinitrate (ISDN), isosorbide 5-mononitrate (IS5N), cyclosine, N-nitratopivaloyl-S-(N'-acetylalanyl)cysteine ethyl ester (SPM-5185) and arginine oligomers comprising from 1 to 5 amino acids.

16. Composition according to either of Claims 14 and 15, characterized in that said agent is present in the composition in an amount ranging from 0.001 to 10% by weight relative to the total weight of the composition, preferably from 0.01 to 5%, and even more preferentially from 0.01 to 2% by weight relative to the total weight of the composition.

17. Composition according to any one of Claims 14 to 16, characterized in that said agent is combined, in the composition, with at least one makeup agent with an optical volume effect on the lips, such as goniochromatic pigments, reflective particles and mixtures thereof.

18. Composition according to any one of Claims 14 to 17, characterized in that the composition also comprises at least one agent chosen from fillers, dyestuffs, cosmetic active agents, thickeners, surfactants, moisturizers, softeners, sequestering agents, fragrances, neutralizing agents, preserving agents, antioxidants, UV-screening agents,

bactericides, trace elements, and mixtures thereof.

19. Composition according to any one of Claims 14 to 18, characterized in that said agent is adsorbed or incorporated into particles having a size ranging from 1 nm to 10 μm.

20. Cosmetic process aimed at making the lips naturally full and/or coloured, characterized in that a composition as defined in Claims 14 to 19 is applied to the lips.

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2006/002659

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61Q1/04 A61Q1/06 A61Q19/00 A61K8/40 A61K8/19
A61K8/97

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61K A61Q

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

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, PAJ, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 572 848 B1 (BRETON LIONEL ET AL) 3 June 2003 (2003-06-03) column 3, lines 15-22,30-60 column 4, lines 8-61 column 5, lines 8-20; claims; example 2	1-20
X	EP 1 080 730 A (TAISHO PHARMACEUTICAL CO., LTD) 7 March 2001 (2001-03-07) examples	1-20
X	PATENT ABSTRACTS OF JAPAN vol. 014, no. 188 (C-0710), 17 April 1990 (1990-04-17) & JP 02 032006 A (SHISEIDO CO LTD), 1 February 1990 (1990-02-01) abstract	1-20

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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
31 May 2006	14/06/2006

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INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2006/002659

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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X	US 6 380 263 B1 (PRUCHE FRANCIS ET AL) 30 April 2002 (2002-04-30) the whole document	1-20

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2006/002659

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