P/00/008b 12/11/91
Section 29 (1)
Regulation 3.1 (2)

AUSTRALIA

Patents Act 1990

NOTICE OF ENTITLEMENT

(To be filed before acceptance)

We, **L'OREAL**, of 14 rue Royale, F-75008 Paris, France, being the applicant in respect of Application No. 36372/93 state the following:-

The Person nominated for the grant of the patent has entitlement from the actual inventors by assignment.

The person nominated for the grant of the patent is the applicant of the application listed in the declaration under Article 8 of the PCT.

The basic application listed on the request form is the first application made in a Convention country in respect of the invention.

By our Patent Attorneys,
WATERMARK PATENT & TRADEMARK ATTORNEYS

.....

20 March 1996

Louis C. Gebhardt
Registered Patent Attorney

AU9336372

(12) PATENT ABRIDGMENT (11) Document No. AU-B-36372/93
(19) AUSTRALIAN PATENT OFFICE (10) Acceptance No. 669159

(54) Title
COSMETIC COMPOSITION CONTAINING MELANISTIC PIGMENTS IN ASSOCIATION WITH CERTAIN TOCOPHEROLS, AND METHOD FOR PROTECTING THE SKIN, THE HAIR, THE MUCOUS MEMBRANES AND COSMETIC COMPOSITIONS

(51)[5] International Patent Classification(s)
A61K 007/48 **A61K 007/13** **A61K 007/16** **A61K 007/18**
A61K 007/42 **A61K 007/44** **A61K 007/021** **A61K 007/032**

(21) Application No. : **36372/93** (22) Application Date : **02.03.93**

(87) PCT Publication Number : **WO93/17659**

(30) Priority Data

(31) Number	(32) Date	(33) Country
92 02532	**03.03.92**	**FR FRANCE**

(43) Publication Date : **05.10.93**

(44) Publication Date of Accepted Application : **30.05.96**

(71) Applicant(s)
L'OREAL

(72) Inventor(s)
ISABELLE HANSENNE; SERGE FORESTIER; QUANG LAN N'GUYEN

(74) Attorney or Agent
WATERMARK PATENT & TRADEMARK ATTORNEYS , Locked Bag 5, HAWTHORN VIC 3122

(57) Claim

1. Cosmetic composition characterized in that it comprises the combination of at least one tocopherol chosen from α-tocopherol, β-tocopherol, γ-tocopherol, δ-tocopherol and their isomers with at least one melanin-like pigment derived from natural or synthetic sources, in a cosmetically acceptable carrier.

19. Method for protecting the human epidermis, the mucosae and the hair against free radicals, characterized in that it consists in applying to the latter an effective quantity of a cosmetic composition according to any one of claims 1 to 18.

OPI DATE 05/10/93 APPLN. ID 36372/93
AOJP DATE 09/12/93 PCT NUMBER PCT/FR93/00207

AU9336372

DEMANDE INTERNATIONALE PUBLIEE EN VERTU DU TRAITE DE COOPERATION EN MATIERE DE BREVETS (PCT)

(51) Classification internationale des brevets 5 :		(11) Numéro de publication internationale: WO 93/17659
A61K 7/42, 7/48, 7/13	A1	(43) D.. de publication internationale: 16 septembre 1993 (16.09.93)

(21) Numéro de la demande internationale: PCT/FR93/00207

(22) Date de dépôt international: 2 mars 1993 (02.03.93)

(30) Données relatives à la priorité:
92/02532 3 mars 1992 (03.03.92) FR

(71) Déposant: L'OREAL [FR/FR]; 14, rue Royale, F-75008 Paris (FR).

(72) Inventeurs: HANSENNE, Isabelle ; 156-158, rue Legendre, F-75017 Paris (FR). FORESTIER, Serge ; 16, allée Ferdinand-Buisson, F-77410 Claye-Souilly (FR). N'GUYEN, Quang, Lan ; 45, avenue Alsace-Lorraine, F-92160 Antony (FR).

(74) Mandataire: BUREAU D.A. CASALONGA JOSSE; 8, avenue Percier, F-75008 Paris (FR).

(81) Etats désignés: AU, CA, JP, brevet européen (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Publiée
Avec rapport de recherche internationale.

669159

(54) Title: COSMETIC COMPOSTION CONTAINING MELANISTIC PIGMENTS IN ASSOCIATION WITH CERTAIN TOCOPHEROLS, AND METHOD FOR PROTECTING THE SKIN, THE HAIR, THE MUCOUS MEMBRANES AND COSMETIC COMPOSITIONS

(54) Titre: COMPOSITION COSMETIQUE CONTENANT DES PIGMENTS MELANIQUES EN ASSOCIATION AVEC CERTAINS TOCOPHEROLS, ET PROCEDE DE PROTECTION DE LA PEAU, DES CHEVEUX, DES MUQUEUSES ET DES COMPOSITIONS COSMETIQUES

(57) Abstract

The present invention relates to a cosmetic composition comprising the association of certain tocopherols bn with at least one melanistic pigment derived from natural or synthetic sources, in a cosmetically acceptable vehicle as well as a method for the protection of the skin, the mucuous membranes, the hair and cosmetic compositions against free radicals.

(57) Abrégé

La présente invention concerne une composition cosmétique comprenant l'association de certains tocophérols bn avec au moins un pigment mélanique, dérivé de sources naturelles ou synthétiques, dans un support cosmétiquement acceptable ainsi qu'un procédé de protection de la peau, des muqueuses, des cheveux et des compositions cosmétiques contre les radicaux libres.

Cosmetic composition containing melaninlike pigments in combination with certain tocopherols, and process for protecting the skin, hair, mucosae and cosmetic compositions.

The present invention relates to a cosmetic composition comprising melaninlike pigments in combination with certain tocopherols, aimed especially at protecting the human epidermis, the mucosae and the hair against free radicals, and to a process for protecting the human epidermis, the mucosae and the hair and cosmetic compositions against these radicals.

Solar radiation, heat, atmospheric pollution and especially smoke and tobacco are known to result in the formation of free radicals. These free radicals initiate degradation reactions of the lipids, proteins and nucleic acids which are present especially in the skin, the mucosae and hair. In addition, cosmetic compositions include constituents which are sensitive to free radicals, and especially lipids.

It has therefore appeared particularly important to protect the skin, the mucosae and hair from these free radicals.

Vitamin E is a known antioxidant for protecting the phospholipids of the cell membrane (J. B. Chazan and M. Szulc - Radicaux Libres et Vitamine E [Free Radicals and Vitamin E], Cah. Nutr. Diet. 1987, XXII, 1, pages 66-76) and its properties as agents against free radicals (AFR) are known.

Furthermore, certain melaninlike pigments have already been employed in cosmetic compositions for protecting the human epidermis against UV rays, making-up the skin, the eyelashes and the eyebrows or else coloring the hair, where their protective role against solar radiation has been established.

According to the invention it has been surprisingly discovered that the combination of melaninlike pigments with certain tocopherols, in a cosmetic

composition, makes it possible to obtain very good results in terms of activity against free radicals. The activity of the combination against free radicals is, in fact, more active than each of the components, vitamin E, on the one hand, or the melaninlike pigments, on the other hand, when the latter are taken separately, at comparable concentrations.

The subject of the present invention is therefore a cosmetic composition comprising the combination of certain tocopherols with at least one melaninlike pigment, in a cosmetically acceptable carrier.

The tocopherols according to the invention are chosen from α-tocopherol, β-tocopherol, γ-tocopherol and δ-tocopherol and their isomers. α-Tocopherol, preferred according to the invention, is vitamin E. It exists in the forms of D-α-tocopherol, L-α-tocopherol and DL-α-tocopherol. DL-α-tocopherol is marketed in particular by Hoffmann La Roche. A mixture of α-tocopherol, β-tocopherol, γ-tocopherol and δ-tocopherol in a ratio of 25/25/25/25, dissolved in soya oil at a concentration of 50 % is marketed under the name "Tocopherol Concentrat Naturel" by Rossow.

The activity against free radicals, which is improved in the combination according to the invention when compared with the activity of vitamin E, on the one hand, or that of the melaninlike pigments, on the other hand, has been demonstrated by the "Head Space" method (Q.L. N-Guyen et al., Symposium of AFECG-SFC, Bordeaux, May 1984, p. 358-359, Evaluation de l'oxydation aldéhydique dans les produits cosmétiques [Evaluation of aldehyde oxidation in cosmetic products]; K. Warner et al., Journal of Food Science, 1974, V.39, p.761-765, Pentane formation and rancidity in vegetable oils). This method makes it possible to evaluate the percentage inhibition of the oxidation of vitamin F, itself highly oxidizable, by the product to be tested.

Melaninlike pigments have a mean diameter of between 10 nm and 50,000 nm, preferably between 30 nm and

20,000 nm.

The melaninlike pigment(s) are derived from natural or synthetic sources and can be obtained (A) by oxidation of at least one indolelike compound, (B) by oxidizing or enzymatic polymerization of melaninlike precursors, (C) by extraction of melanin from natural substances containing it, or (D) by culture of micro-organisms which produce melanin.

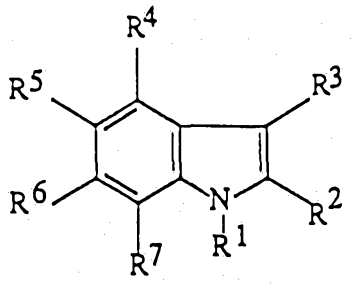
The tocopherols of the invention are advantageously present in the cosmetic composition according to the invention by themselves or mixed, in a concentration of between 0.02 and 10 % by weight relative to the total weight of the composition, and preferably between 0.02 % and 6 %.

The melaninlike pigments are advantageously present in the cosmetic composition according to the invention in a concentration of between 0.001 and 2 %, preferably between 0.005 and 0.5 % by weight relative to the total weight of the composition.

The tocopherol/melaninlike pigment weight ratio may be envisaged between 0.1 and 100, preferably 0.5 to 50.

According to the invention the pigments may be chosen from melaninlike pigments obtained by oxidation of an indolelike compound, by oxidizing or enzymatic polymerization of melaninlike precursors, by extraction of melanin from natural substances or by culture of micro-organisms which produce melanin.

(A) In the first place, the melaninlike pigments can be obtained by oxidation of at least one indolelike compound chosen especially from those corresponding to the formula (I):



(I)

in which:

- R^1 and R^3 denote, independently of one another, a hydrogen atom or a C_1-C_4 alkyl group;
- R^2 denotes a hydrogen atom, a C_1-C_4 alkyl group, a carboxyl group or a C_1-C_4-alkoxycarbonyl group;
- R^4 and R^7 denote, independently of one another, a hydrogen atom, a hydroxyl group, a C_1-C_4 alkyl group, an amino group, a C_1-C_4 alkoxy group, a C_2-C_4 acyloxy group or a C_2-C_4 acylamino group;
- R^5 denotes a hydrogen atom, a hydroxyl group, a C_1-C_4 alkoxy group, a C_1-C_4 alkyl group, a halogen atom, an amino group, a C_2-C_{14} acyloxy group, a C_2-C_4 acylamino group or a trimethylsilyloxy group;
- R^6 denotes a hydrogen atom, a hydroxyl group, a C_1-C_4 alkoxy group, an amino group, a C_2-C_4 acyloxy group, a C_2-C_4 acylamino group, a trimethylsilyloxy group or a C_2-C_4 hydroxyalkylamino group;
- it being also possible for R^5 and R^6 to form, together with the carbon atoms to which they are attached, a methylenedioxy ring optionally substituted by a C_1-C_4 alkyl or C_1-C_4 alkoxy group, or else a carbonyldioxy ring;
- at least one of the radicals R^4 to R^7 denotes a group OZ or NHR^0, not more than one of the radicals R^4 to R^7 denoting NHR^0 and not more than two of the radicals R^4 to R^7 denoting OZ and, in the case where Z denotes a hydrogen atom, the two OH groups are in positions 5 and 6; and at least one of the radicals R^4 to R^7 denotes a hydrogen atom, and in the case where only one of these radicals denotes a hydrogen atom, only one radical among the radicals R^4 to R^7 then denotes NHR^0 or OZ, the other radicals denoting a C_1-C_4 alkyl group;

- the radical R^0 of the group NHR^0 denoting a hydrogen atom, a C_2-C_4 acyl or C_2-C_4 hydroxyalkyl group, and the radical Z of the group OZ denoting a hydrogen atom, a C_2-C_{14} acyl group, a C_1-C_4 alkyl group or a trimethylsilyl group,

and their alkali metal, alkaline-earth metal, ammonium or amine salts.

The indolelike compounds of formula (I) above are preferably chosen from 4-hydroxyindole, 5-hydroxyindole, 6-hydroxyindole, 7-hydroxyindole, 4-hydroxy-5-methoxyindole, 4-hydroxy-5-ethoxyindole, 2-carboxy-5-hydroxyindole, 5-hydroxy-6-methoxyindole, 6-hydroxy-7-methoxyindole, 5-methoxy-6-hydroxyindole, 5,6-dihydroxyindole, N-methyl-5,6-dihydroxyindole, 2-methyl-5,6-dihydroxyindole, 3-methyl-5,6-dihydroxyindole, 2,3-dimethyl-5,6-dihydroxyindole, 2-carboxy-5,6-dihydroxyindole, 4-hydroxy-5-methylindole, 2-carboxy-6-hydroxyindole, 6-hydroxy-N-methylindole, 2-ethoxycarbonyl-5,6-dihydroxyindole, 4-hydroxy-7-methoxy-2,3-dimethylindole, 4-hydroxy-5-ethoxy-N-methylindole, 6-hydroxy-5-methoxy-2-methylindole, 6-hydroxy-5-methoxy-2,3-dimethylindole, 6-hydroxy-2-ethoxycarbonylindole, 7-hydroxy-3-methylindole, 5-hydroxy-6-methoxy-2,3-dimethylindole, 5-hydroxy-3-methylindole, 5-acetoxy-6-hydroxyindole, 5-hydroxy-2-ethoxycarbonylindole, 6-hydroxy-2-carboxy-5-methylindole, 6-hydroxy-2-ethoxycarbonyl-5-methoxyindole, 6-N-β-hydroxyethylaminoindole, 4-aminoindole, 5-aminoindole, 6-aminoindole, 7-aminoindole, N-methyl-6-β-hydroxyethylaminoindole, 6-amino-2,3-dimethylindole, 6-amino-2,3,4,5-tetramethylindole, 6-amino-2,3,4-trimethylindole, 6-amino-2,3,5-trimethylindole, 6-amino-2,3,6-trimethylindole, 5,6-diacetoxyindole, 5-methoxy-6-acetoxyindole, 5,6-dimethoxyindole, 5,6-methylenadioxyindole, 5,6-trimethylsilyloxyindole, the phosphoric ester of 5,6-dihydroxyindole, 5,6-dibenzyloxyindole, and the addition salts of these compounds.

5,6-Dihydroxyindole is particularly preferred.

The oxidation of the indolelike compound of formula (I) may be performed in an aqueous or water-solvent(s) medium, in air, and in the presence or otherwise of an alkaline agent and/or of a metallic oxidation catalyst such as, for example, the cupric ion.

The reaction medium preferably consists of water and may, if appropriate, consist of a mixture of water and of at least one solvent chosen so that it rapidly dissolves the indolelike compound of formula (I). Among these solvents there may be mentioned, by way of examples, lower C_1-C_4 alcohols such as ethyl alcohol, propyl or isopropyl alcohol, tert-butyl alcohol, alkylene glycols such as ethylene glycol, propylene glycol, alkylene glycol alkyl ethers such as ethylene glycol monomethyl, monoethyl and monobutyl ethers, propylene glycol and dipropylene glycol monomethyl ethers and methyl lactate.

The oxidation may also be performed by using hydrogen peroxide in the presence of an alkaline agent such as, preferably, aqueous ammonia, or in the presence of an iodide ion, the iodide being preferably an alkali metal, alkaline-earth metal or ammonium iodide.

The oxidation may also be undertaken by employing periodic acid and its water-soluble salts and derivatives, permanganates and dichromates such as those of sodium or potassium, sodium hypochlorite, potassium ferricyanide, ammonium persulfate, silver oxide, lead oxide, ferric chloride, sodium nitrite, rare-earth salts including especially those of cerium, and organic oxidizing agents chosen from ortho- and para-benzoquinones, ortho- and para-benzoquinone mono- or diimines, 1,2- and 1,4-naphthoquinones, and 1,2- and 1,4-naphthoquinone mono- or diimines such as defined in Application EP-A-0,376,776. The preferred periodic acid salt is sodium periodate.

It is possible to activate the oxidizing agents using a pH modifier.

An enzymatic oxidation can also be envisaged.

The insoluble product is isolated by filtration, centrifuging, freeze-drying or spray-drying. It is then ground or micronized to reach the desired particle size.

(B) The melaninlike pigments according to the invention can also originate from the oxidizing or enzymatic polymerization of melaninlike precursors such as L-tyrosine, L-dopa, catechol and their derivatives.

(C) The melaninlike pigments according to the invention can also originate from the extraction of melanin from natural substances such as human hair, the ink of cephalopods (cuttlefish, octopuses), also known by the name of sepiomelanin, in which case the pigment is ground and purified before being employed.

(D) Finally, the melaninlike pigments according to the invention can be obtained by culture of microorganisms. These microorganisms produce melanin either naturally or by genetic modification or by mutagenesis. Methods of preparations of these melanins are described, for example, in Patent Application WO90/04029.

The melaninlike pigment(s) may be present at the surface or incorporated into an inorganic or organic, inert particulate filler, to constitute a synthetic composite melaninlike pigment formed in situ. In this case the melaninlike pigment(s) may result from the oxidation of at least one indolelike compound of formula (I), as defined above, mixed with the filler in a medium which is essentially a nonsolvent for the said filler, at a temperature which can range from room temperature to approximately 100°C, or else can result from the oxidizing polymerization of melaninlike precursors on the filler.

The general conditions for the oxidation of the indolelike compounds of formula (I) are the same as those mentioned above.

According to a first embodiment, the particulate filler is an inert inorganic filler advantageously consisting of particles with a particle size smaller than 20,000 nm. Such composite melaninlike pigments deposited

on an inorganic filler are described, as is their preparation, in French Patent Application FR-A-2,618,069.

According to a second embodiment of the present invention, the particulate filler is an inert polymeric filler advantageously chosen from organic or inorganic, natural or synthetic polymers with a crystalline or amorphous, crosslinked network, which has a molecular weight of between 5000 and 5,000,000. Composite melanin-like pigments on a polymeric filler and their preparation are described in Luxembourgian Patent No. 87,429.

The organic or synthetic polymers are, in particular, chosen from the polymers derived from keratin, silk fibroin, chitin or cellulose, or from polyamides or the homo- or copolymers resulting from the polymerization of aliphatic or aromatic, mono- or polyethylenic monomers, with a crystalline or amorphous, crosslinked network.

The cellulosic polymers are chosen more particularly from microcrystalline celluloses such as the products sold under the name "Avicel" by FMC Corporation.

Among the synthetic polymers there may be more particularly mentioned polyethylene, polypropylene, polystyrene, poly(methyl methacrylate) sold under the names "Micropearl M" and "Micropearl M100" by Seppic, crosslinked poly(methyl methacrylate) such as the product sold under the name of "Micropearl M 305" by Seppic. Other polymers are chosen, in particular, from crosslinked poly-β-alanine such as described in French Patent 2,530,250, in which the degree of crosslinking is between 1 and 15 % and, preferably, between 1 and 8 %.

It is also possible to employ, as polymers, the products known under the name of microsponges, such as crosslinked styrene/divinylbenzene or methyl methacrylate/ethylene glycol dimethacrylate or vinyl stearate/divinylbenzene polymers, such as are described in Patents WO-88/01,164 and US-A-4,690,825. Such polymers consist essentially of beads of crosslinked polymers comprising an internal pore network capable of retaining

the melaninlike pigment.

According to a third embodiment the particulate filler is a filler consisting of organic or inorganic particles with a lamellar structure which are smaller than 50,000 nm in size. The particles of lamellar structure consist of leaflets in the case of which the ratio between the longest dimension and the thickness is particularly between 2 and 100.

Composite melaninlike pigments deposited on a lamellar filler, and their preparation, are described in European Patent Application No. 0,467,767.

The cosmetic composition of the invention may be employed as a composition for protecting the human epidermis, the mucosae or the hair, as a product for making-up the skin or its apparent superficial growths. The tocopherol/melaninlike pigment combination is also useful for protecting cosmetic compositions themselves against free radicals; it is also useful in compositions for oral and dental use, such as toothpastes.

This composition can, in particular, take the form of a lotion, thickened lotion, gel, vesicular dispersion, dispersion of nanoparticles, cream, milk, powder, ointment or solid stick and may optionally be packaged as an aerosol and be in the form of a foam or spray.

The compositions in accordance with the invention may be in the form of a vesicular dispersion of ionic or nonionic amphiphilic lipids. They are prepared especially by swelling lipids in an aqueous solution to form spherules dispersed in the aqueous medium, as described in the paper by Bangham, Standish & Watkins, J.Mol. Biol., 13, 238 (1965) or in the Applicant's patents FR-2,315,991 and 2,416,008.

The various types of processes of preparation are described in "Les liposomes en biologie cellulaire et pharmacologie" ["Liposomes in cell biology and pharmacology"], published by INSERM/John Liberry Eurotext, 1987, pages 6 to 18.

The compositions may be in the form of dispersions of nanoparticles. The term "nanoparticles" covers, on the one hand, nanospheres and, on the other hand, nanocapsules; the term "nanospheres" is used to denote the nanoparticles consisting of a porous polymeric matrix on which the active principle is absorbed and/or adsorbed, and the term "nanocapsules" the nanoparticles consisting of a polymeric membrane which surrounds a core formed by the active principle. Such forms of composition are described, for example, in Patent Applications EP-274,961 and FR-2,659,554.

It may contain cosmetic adjuvants which are usually employed, such as fatty substances, organic solvents, silicones, thickeners, emollients, UV-A, UV-B or broad-band sunscreens, antifoam agents, hydrating agents, perfumes, stabilizers, surfactants, fillers, sequestrants, anionic, cationic, nonionic or amphoteric polymers or mixtures thereof, propellants, alkalifying or acidifying agents, dyes, metal oxide pigments such as iron oxides, or any other ingredient usually employed in cosmetics, as well as self-tanning agents such as dihydroxyacetone.

Among the organic solvents there may be mentioned lower alcohols and polyols such as ethanol, isopropanol, propylene glycol, glycerin and sorbitol. Esters of fatty acids, such as isopropyl myristate, isopropyl adipate, benzoates of C_{12}-C_{15} fatty alcohols ("Finsolv TN" from Finetex), myristyl alcohol oxypropylenated with 3 moles of propylene oxide ("Witconol APM" from Witco), and the like, and triglycerides of capric and caprylic acids ("Miglyol 812" from Hüls).

The cosmetic composition according to the invention may therefore contain thickeners which can be chosen from acrylic acid polymers, crosslinked or otherwise, and particularly the polyacrylic acids crosslinked with a polyfunctional agent, such as the products sold under the name "Carbopol" by Goodrich, cellulose derivatives such as methyl cellulose, hydroxyethyl cellulose, hydroxy-

propyl methyl cellulose, sodium salts of carboxymethyl cellulose, and mixtures of cetyl stearyl alcohol and of cetyl stearyl alcohol oxyethylenated with 33 moles of ethylene oxide.

It is also possible to employ the products resulting from the ionic interaction of a cationic polymer consisting of a copolymer of cellulose and of a cellulose derivative which are grafted with a salt of a water-soluble quaternary ammonium monomer and of a carboxylic anionic polymer, such as are described in French Patent FR-2,598,611. Use is preferably made of the product of ionic interaction of a hydroxyethyl cellulose copolymer grafted by a radical route with diallyldimethylammonium chloride, such as the polymer marketed under the name "Celquat L 200" by National Starch, either with copolymers of ethylene and maleic anhydride such as the products sold under the name "EMA 31" by Monsanto, or with 50/50 copolymers of methacrylic acid and methyl methacrylate.

Another product of this type which can be employed is the product resulting from the ionic interaction of the copolymer of hydroxyethyl cellulose grafted by a radical route with diallyldimethylammonium chloride with a crosslinked carboxylic anionic polymer, such as the crosslinked copolymers of methacrylic acid and ethyl acrylate which are sold under the name "Viscoatex" 538 or 46 by Coatex.

The fatty substances may consist of an oil or a wax or a mixture thereof, fatty acids, fatty alcohols, vaseline, paraffin, lanolin, hydrogenated lanolin, acetylated lanolin, cocoa butter or karité butter.

The oils are chosen from animal, vegetable, mineral or synthetic oils, and especially hydrogenated palm oil, hydrogenated castor oil, vaseline oil, liquid paraffin, purcellin oil, silicone oils and isoparaffins.

The waxes are chosen from animal, fossil, vegetable, mineral or synthetic waxes. Beeswaxes, carnauba and candelilla, sugar cane and Japan waxes, ozokerites,

montan wax, microcrystalline waxes, paraffin waxes and silicone waxes and resins may be mentioned in particular.

When the cosmetic composition according to the invention is employed for protecting the human epidermis, it may take the form of suspension or dispersion in solvents or fatty substances, or else the form of emulsion such as a cream or a milk, the form of ointment, gel, solid stick or of aerosol foam.

The emulsions may additionally contain anionic, nonionic, cationic or amphoteric surface-acting agents.

The composition for protecting the human epidermis against free radicals may additionally contain antisolar or self-tanning agents and, in the same forms as above, can be employed as a protective antisolar or self-tanning composition.

When the cosmetic composition according to the invention is employed for the protection of hair, it can take the form of a shampoo, lotion, rinsing gel or composition, to be applied before or after shampooing, before or after dyeing or bleaching, before, during or after permanent waving or straightening, styling or treating lotion or gel, lotion or gel for blow drying or setting, hair lacquer, permanent wave or hair straightening, dyeing or bleaching composition.

When the composition is employed as a make-up product for eyelashes, eyebrows or the skin, such as a cream for treating the epidermis, make-up foundation, lipstick, eye shadow, cheek blush, eyeliner or mascara, it can take an anhydrous or aqueous, solid or pasty form, such as oil-in-water or water-in-oil emulsions or suspensions.

When the composition is employed for the make-up of hair, it can also take anhydrous, or aqueous, solid or pasty form, in the form of oil-in-water or water-in-oil emulsions or else in the form of suspensions or gels, such as styling or make-up gels.

When the composition is employed in an oral-dental care composition, it may include adjuvants and

additives which are usual in the case of compositions for oral use and especially surface-active agents, thickening agents, moistening agents and polishing agents such as silica, active agents such as fluorides, and in particular sodium fluoride, and optionally sweetening agents such as sodium saccharinate.

A further subject of the invention is a process for protecting the human epidermis, the mucosae and hair against the detrimental action of free radicals, consisting in applying an effective quantity of the above composition to the latter.

Another subject of the invention is a make-up process consisting in applying the above cosmetic composition to the skin, its apparent superficial growths or the hair.

Another subject of the invention is a process for protecting cosmetic compositions against free radicals, consisting in incorporating therein an effective quantity of the tocopherol/melaninlike pigment combination.

The invention will be illustrated better by the following nonlimiting examples.

EXAMPLE 1

A sun cream of the following composition is prepared:

- Melanin obtained by oxidation of 5,6-dihydroxyindole 0.025 g AS
- DL-α-Tocopherol (vitamin E) sold by Hoffman La Roche 0.5 g
- 2-Ethylhexyl p-methoxycinnamate sold under the name of "Parsol MCX" by Givaudan 5.0 g
- Mixture (80/20) of cetyl stearyl alcohol and of cetyl stearyl alcohol oxyethylenated with 33 moles of ethylene oxide, sold under the name "Sinnowax AO" by Henkel 7.0 g
- Glycerol mono- and distearate (40/50) sold under the name "Geleol" by Gattefosse 2.0 g

- Cetyl alcohol (90 % C_{16}) 1.5 g
- Vaseline oil 15.0 g
- Polydimethylsiloxane 1.5 g
- Glycerin 3.0 g
- Stabilizers, perfume q.s.
- Water q.s. 100 g

EXAMPLE 2

A self-tanning cream of the following composition is prepared:

- Melanin obtained by oxidation of 5,6-dihydroxyindole 0.015 g AS
- DL-α-Tocopherol (vitamin E) sold by Hoffmann La Roche 1.0 g
- Dihydroxyacetone 3.0 g
- Mixture (80/20) of cetyl stearyl alcohol and of cetyl stearyl alcohol oxyethylenated with 33 moles of ethylene oxide, sold under the name "Sinnowax AO" by Henkel 7.0 g
- Glycerol mono- and distearate (40/50) sold under the name "Geleol" by Gattefosse 2.0 g
- Cetyl alcohol (90 % C_{16}) 1.5 g
- Vaseline oil 10.0 g
- Polydimethylsiloxane 1.5 g
- Glycerin 10.0 g
- Stabilizers, perfume q.s.
- Water q.s. 100 g

EXAMPLE 3

A hair make-up gel of the following composition is prepared:

- Crosslinked methacrylic acid/ethyl acrylate copolymer in anionic dispersion at a concentration of 38 % AS in water, marketed under the name "Viscoatex 538" by Coatex 1.6 g AS
- Hydroxyethyl cellulose/diallyldimethyl-ammonium chloride copolymer marketed under the name "Celquat L200" by National Starch 1.6 g

- Polydimethylsiloxane containing amino-ethylpropylamine groups in cationic emulsion at a concentration of 35 % AS in water, marketed under the name "DC 929" by Dow Corning	0.3	g AS
- Ethanol	10.0	g
- DL-α-Tocopherol (vitamin E) sold by Hoffmann La Roche	0.1	g
- Melaninlike pigment obtained by oxidation of 5,6-dihydroxyindole	1.0	g
- Stabilizer, sequestrant	q.s.	
- Perfume	q.s.	
- 2-Amino-2-methyl-1-propanol	q.s. pH 7.5	
- Demineralized water	q.s. 100	g

EXAMPLE 4

A toothpaste which has the following composition is prepared:

- Silica marketed under the name "Tixosil 73" by Rhône Poulenc	12.0	g
- Silica marketed under the name "Tixosil 333" by Rhône Poulenc	8.0	g
- Sorbitol in solution at a concentration of 70 % AS in water	14.0	g AS
- Glycerin	5.0	g
- Carboxymethyl cellulose sold under the name "Blanose 9M 31 F" by Hercules	1.4	g
- Sodium lauryl sulfate at a concentration of 92 % of AS in water, sold under the name "Empicol LZV/E" by Marchon	1.8	g
- Sodium fluoride	0.22	g
- Titanium dioxide	0.5	g
- Sodium saccharinate	q.s.	
- Flavoring	q.s.	
- Vitamin E	0.15	g
- Melaninlike pigment obtained by oxidation of 5,6-dihydroxyindole	0.01	g
- Stabilizer	q.s.	
- Water	q.s. 100	g

EXAMPLE 5

A make-up foundation of the following composition is prepared:

A)			
	- Water	44.80	g
	- Methyl p-hydroxybenzoate	0.10	g
	- Propylene glycol	2.00	g
	- Yellow iron oxide	1.00	g
	- Red iron oxide	0.40	g
	- Black iron oxide	0.20	g
	- Titanium oxide	9.40	g
	- Melanin obtained by oxidation of 5,6-dihdyroxy indole	0.01	g
	- Magnesium silicate and aluminum hydrate	1.00	g
	- Sodium lauroyl sarcosinate in water at a concentration of 30 % sold under the name "Oramix L30" by Seppic	0.18	g MA
	- Sodium carboxymethyl cellulose	0.20	g
	- Triethanolamine	1.00	g
B)			
B1	- Stearic acid	2.20	g
	- Mixture of glyceryl mono-di-stearate, stearic acid, glycerin (40/50/5/5) sold under the name "Geleol" by Gattefosse	2.20	g
	- Triglycerides of caprylic acids sold under the name "Miglyol 812" by Hüls	15.00	g
	- Propyl p-hydroxybenzoate	0.30	g
	- Cyclopenta dimethylsiloxane	10.00	g
	- DL-α-tocopherol (vitamin E) sold by Hoffmann La Roche	0.09	g
C)			
	- Water	1.00	g
	- Imidazolidinylurea	0.30	g
	- Glycerin	3.00	g

D)

- Perfume 0.20 g

E)

- Starch crosslinked with octenylsuccinic anhydride, sold under the name "Dry Flo PC" by National Starch 5.00 g

OPERATING METHOD:

1) Heating is carried out in a beaker at 95°C. The propylene glycol is introduced and the methyl para-hydroxybenzoate is dissolved. At 80°C, the pigments are dispersed for 1 hour and then the melanin for 10 minutes. The magnesium silicate and the aluminum hydrate are introduced with stirring. The material is allowed to cool to 70°C and the Oramix L30 and sodium carboxymethyl cellulose and triethanolamine are added.

2) The ingredients of phase B1 are melted at 80°C. The cyclopentadimethyl siloxane and the vitamin E are added to them. The mixture B is maintained at 65°C.

3) Phase B is poured onto phase A with stirring using the turbine. The mixture is allowed to cool with stirring to 40°C and phase C, prepared at a temperature of less than 40°C is added, and then D and E are added with stirring and the temperature is allowed to return to 25°C.

EXAMPLE 6

A mascara of the following composition is prepared:

A
- Triethanolamine stearate 12.0 g
- Beeswax 4.0 g
- Carnauba wax 1.5 g
- Paraffin wax 6.0 g

- DL-α-Tocopherol (vitamin E) sold by Hoffmann La Roche 0.36 g
- Black iron oxide 5.0 g
- Melanin obtained by oxidation of 5,6-dihydroxyindole 0.04 g

B	- Hydroxyethyl cellulose	1.5	g
	- Gum arabic	1.0	g
	- Polyvinylpyrrolidone	1.0	g
	- Methyl para-hydroxybenzoate	0.2	g
	- Propyl para-hydroxybenzoate	0.7	g
	- Water q.s.	100	g

OPERATING METHOD:

The components of phase A are heated to 85°C, the iron oxides and the melanin are added and mixing is then carried out using the turbine.

The water for the preparation is boiled and the stabilizers are dissolved in it and then, at 85°C, the components of phase B are added.

The aqueous phase at 85°C is added to phase A (80°C), into which the vitamin E has been introduced while mixing using the turbine. The material is cooled while mixing to 27°C.

EXAMPLE 7

An antisun cream of the following composition is prepared:

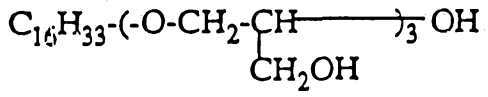
- Melanin obtained by oxidation of 5,6-dihydroxyindole	0.08	g
- Mixture of natural tocopherols in soya oil (50/50) sold under the name "Tocopherol Concentrat Naturel" by Rossow	0.04	g
- 2-Ethylhexyl p-methoxycinnamate sold under the name "Parsol MCX" by Givaudan	5.0	g
- Cetyl alcohol (90% C_{16})	15.0	g
- Polyethylene glycol monostearate containing 50 moles of ethylene oxide, sold under the name "Myrj 53" by ICI	3.0	g
- Glycerol mono- and distearate (40/50) sold under the name "Geleol" by Gattefosse	3.0	G [sic]
- Vaseline oil	24.0	g
- Water q.s	100	g

EXAMPLE 8

A face cream of the following composition is prepared:

First phase:

- Nonionic amphiphilic lipid of general formula:



3.8 g

- Cholesterol 3.8 g
- Dicetyl phosphate 0.4 g
- DL-α-Tocopherol (vitamin E) sold by Hoffmann La Roche 0.05 g
- Glycerol 3.0 g
- Melanin obtained by oxidation of 5,6-dihydroxyindole 0.01 g
- Stabilizers q.s. 0.01 g
- Water 52.44 g

Second phase:

- Macadamia oil 15.0 g
- Perfume q.s.
- Crosslinked polyacrylic acid sold under the name "Carbopol 940" by Goodrich 0.4 g
- Triethanolamine 0.4 g
- Water 20.0 g

The first phase is prepared as follows: the lipids are mixed at 95°C in the molten state. Vitamin E is added to them. The aqueous phase (glycerol + water) is heated to 80°C. Part of the aqueous phase is mixed into the lipid phase with gentle stirring to form a lamellar phase. The remainder of the aqueous phase is added to form the dispersion phase. The melanin and the stabilizers are added. Stirring is continued until a concentrated vesicular suspension is obtained. This is homogenized in order to reduce the size of the vesicles (mean diameter around 200 nm).

The second phase is then added, the macadamia oil being first dispersed by mechanical stirring at 40°C, then the perfume, the "Carbopol 940", the triethanolamine and the water being incorporated.

EXAMPLE 9

A body cream of the following compositon is prepared:

1) Preparation of a dispersion of nanoparticles

250 mg of a condensate of ethylene oxide and propylene oxide (20/80 %), with a mean molecular weight of 1750 and 8350 respectively, sold under the trade name of "Pluronic F68" by BASF, are dissolved in 50 ml of demineralized water in a 100-ml beaker, with stirring provided by a magnetic bar rotating at 400 rev/min. Into this aqueous phase, thermostatted at a temperature of 40°C, are slowly poured 25 ml of acetone, in which 250 mg of soya lecithin, sold under the trade name "Epikuron 170" by Lucas Meyer have been previously dissolved at a temperature of 55°C, and then, after returning to a temperature of 40°C, the following are dissolved:

- 500 mg of a tocopherol mixture in soya oil (50/50) sold under the name "Tocopherol Concentrat Naturel" by Rossow.
- 125 mg of polycaprolactone marketed by Aldrich.

Stirring is maintained for 2 hours at a temperature of 40°C, followed by a return to room temperature. The nanoparticle dispersion obtained is then transferred into a 250-ml round bottom flask which is placed on a rotary evaporator and the acetone is evaporated off. A fluid, colloidal dispersion of nanoparticles whose mean diameter is 195 nm is thus obtained.

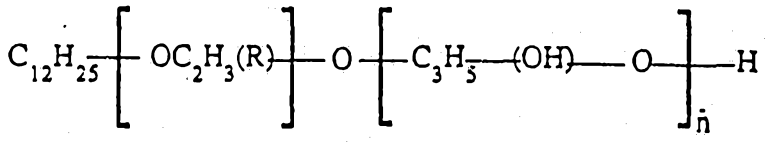
On examination with a microscope, in white light, a dense population of nanoparticles which are uniform in size is observed.

2) Preparation of a dispersion of vesicles

0.05 g of dimyristyl phosphate and 0.95 g of nonionic surfactant of formula (I) are weighed into a

100-ml glass beaker:

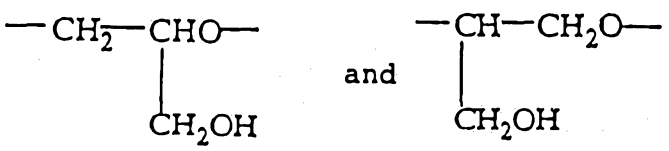
- Nonionic lipid of formula:



in which formula:

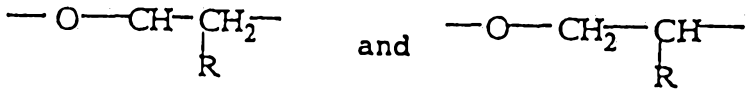
* $-C_3H_5(OH)O-$

consists of a mixture of radicals:



* $-O-C_2H_3(R)-$

consists of a mixture of radicals



* $\bar{n}$ is a mean statistical value equal to 2.7, determined by ^{1}HNMR at 500 MHz,

* R is a mixture of radicals $C_{14}H_{29}$ and $C_{16}H_{33}$

These two lipids are homogenized by heating on a hotplate at a temperature of 100°C and the mixture is then cooled to 40°C. 27.575 g of water in which 3 g of glycerin and 0.02 g of citric acid have previously been dissolved are then added. The whole is homogenized by the action of an ultradisperser of "Virtis" type for 2 minutes at a speed of 40,000 rev/min, at a temperature of 40°C. 3 g of water are then added, in which 0.1 g of stabilizer sold under the trade name "Kathon CG" by Rhom [sic] & Haas and 0.2 g of stabilizer sold under the trade name "Germal 115" by Rhom [sic] & Haas and 0.025 g of melanin obtained by oxidation of 5,6-dihydroxyindole have previously been dissolved.

The fatty phase made up of a mixture of the following products is then added:

- Macadamia oil	9.0	g
- Poultry [sic] silicone oil	7.0	g
- Ethylhexyl para-methoxycinnamate sold under the trade name "Parsol MCX" by Givaudan	0.5	g
- 2-Hydroxy-4-methoxybenzophenone sold under the trade name "Uvinul M 40" by BASF	0.5	g
- Propyl para-hydroxybenzoate	0.05	g

The whole is subjected to the action of the "Virtis" ultradisperser for 5 minutes at room temperature.

3) Mixture of the vesicle and nanoparticle dispersions

20 g of the aqueous dispersion of nanoparticles, prepared previously, are added to the dispersion of vesicles. 35 g of water are then added, in which 0.65 g of carboxyvinylic acid sold under the trade name "Carbopol 940" by Goodrich have been swollen. After homogenization, 0.65 g of triethanolamine diluted with 1.73 g of water are finally added. A thick, white cream of glossy appearance, intended for body care, is thus obtained. After an application of this cream, once daily for a fortnight, an improvement in the surface quality of the treated skin is observed.

CLAIMS

1. Cosmetic composition characterized in that it comprises the combination of at least one tocopherol chosen from α-tocopherol, β-tocopherol, γ-tocopherol, δ-tocopherol and their isomers with at least one melanin-like pigment derived from natural or synthetic sources, in a cosmetically acceptable carrier.

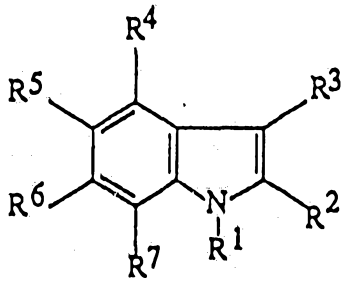
2. Cosmetic composition according to claim 1, characterized in that the tocopherol is vitamin E.

3. Cosmetic composition according to claim 1 or 2, characterized in that the melaninlike pigments are present in the composition in a concentration of between 0.001 and 2 % by weight, and preferably between 0.05 and 0.5 % by weight, relative to the total weight of the composition.

4. Composition according to claim 1, 2 or 3, characterized in that the tocopherol(s) is(are) present in the composition in a concentration of between 0.02 and 10 % by weight, and preferably between 0.02 and 6 % by weight, relative to the total weight of the composition.

5. Cosmetic composition according to any one of claims 1 to 4, characterized in that the melaninlike pigments are obtained by oxidation of at least one indolelike compound, by oxidizing or enzymatic polymerization of melaninlike precursors, by extraction of melanin from natural substances or by culture of microorganisms which produce melanin.

6. Cosmetic composition according to one of claims 1 to 5, characterized in that the melaninlike pigments are obtained by oxidation of at least one indolelike compound of formula:



(I)

in which:

- R^1 and R^3 denote, independently of one another, a hydrogen atom or a C_1-C_4 alkyl group, R^2 denotes a hydrogen atom, a C_1-C_4 alkyl group, a carboxyl group or a C_1-C_4-alkoxycarbonyl group; R^4 and R^7 denote, independently of one another, a hydrogen atom, a hydroxyl group, a C_1-C_4 alkyl group, an amino group, a C_1-C_4 alkoxy group, a C_2-C_4 acyloxy group or a C_2-C_4 acylamino group; R^5 denotes a hydrogen atom, a hydroxyl group, a C_1-C_4 alkoxy group, a C_1-C_4 alkyl group, a halogen atom, an amino group, a C_2-C_{14} acyloxy group, a C_2-C_4 acylamino group or a trimethylsilyloxy group; R^6 denotes a hydrogen atom, a hydroxyl group, a C_1-C_4 alkoxy group, an amino group, a C_2-C_4 acyloxy group, a C_2-C_4 acylamino group, a trimethylsilyloxy group or a C_2-C_4 hydroxyalkylamino group; it being also possible for R^5 and R^6 to form, together with the carbon atoms to which they are attached, a methylenedioxy ring optionally substituted by a C_1-C_4 alkyl or C_1-C_4 alkoxy group, or else a carbonyldioxy ring; at least one of the radicals R^4 to R^7 denotes a group OZ or NHR^0, not more than one of the radicals R^4 to R^7 denoting NHR^0 and not more than two of the radicals R^4 to R^7 denoting OZ and, in the case where Z denotes a hydrogen atom, the two OH groups are in positions 5 and 6; and at least one of the radicals R^4 to R^7 denotes a hydrogen atom, and in the case where only one of these radicals denotes a hydrogen atom, only one radical among the radicals R^4 to R^7 then denotes NHR^0 or OZ, the other radicals denoting a C_1-C_4 alkyl group; the radical R^0 of the group NHR^0 denoting a hydrogen atom, a C_2-C_4 acyl or C_2-C_4 hydroxyalkyl group, and the radical Z of the group OZ denoting a hydrogen atom, a C_2-C_{14} acyl group, a C_1-C_4 alkyl group or a trimethylsilyl group;

and the alkali metal, alkaline-earth metal, ammonium or amine salts of this indolelike compound.

7. Cosmetic composition according to claim 6, characterized in that the indolelike compound is chosen from 4-hydroxyindole, 5-hydroxyindole, 6-hydroxyindole,

7-hydroxyindole, 4-hydroxy-5-methoxyindole, 4-hydroxy-5-ethoxyindole, 2-carboxy-5-hydroxyindole, 5-hydroxy-6-methoxyindole, 6-hydroxy-7-methoxyindole, 5-methoxy-6-hydroxyindole, 5,6-dihydroxyindole, N-methyl-5,6-dihydroxyindole, 2-methyl-5,6-dihydroxyindole, 3-methyl-5,6-dihydroxyindole, 2,3-dimethyl-5,6-dihydroxyindole, 2-carboxy-5,6-dihydroxyindole, 4-hydroxy-5-methylindole, 2-carboxy-6-hydroxyindole, 6-hydroxy-N-methylindole, 2-ethoxycarbonyl-5,6-dihydroxyindole, 4-hydroxy-7-methoxy-2,3-dimethylindole, 4-hydroxy-5-ethoxy-N-methylindole, 6-hydroxy-5-methoxy-2-methylindole, 6-hydroxy-5-methoxy-2,3-dimethylindole, 6-hydroxy-2-ethoxycarbonylindole, 7-hydroxy-3-methylindole, 5-hydroxy-6-methoxy-2,3-dimethylindole, 5-hydroxy-3-methylindole, 5-acetoxy-6-hydroxyindole, 5-hydroxy-2-ethoxycarbonylindole, 6-hydroxy-2-carboxy-5-methylindole, 6-hydroxy-2-ethoxycarbonyl-5-methoxyindole, 6-N-β-hydroxyethylaminoindole, 4-aminoindole, 5-aminoindole, 6-aminoindole, 7-aminoindole, N-methyl-6-β-hydroxyethylaminoindole, 6-amino-2,3-dimethylindole, 6-amino-2,3,4,5-tetramethylindole, 6-amino-2,3,4-trimethylindole, 6-amino-2,3,5-trimethylindole, 6-amino-2,3,6-trimethylindole, 5,6-diacetoxyindole, 5-methoxy-6-acetoxyindole, 5,6-dimethoxyindole, 5,6-methylenedioxyindole, 5,6-trimethylsilyloxyindole, the phosphoric ester of 5,6-dihydroxyindole, 5,6-dibenzyloxyindole, and the addition salts of these compounds.

8. Cosmetic composition according to claim 6 or 7, characterized in that the indolelike compound is 5,6-dihydroxyindole.

9. Cosmetic composition according to any one of claims 1 to 8, characterized in that the melaninlike pigment is a synthetic composite melaninlike pigment deposited at the surface or incorporated into an inorganic or organic, inert particulate filler.

10. Cosmetic composition according to claim 9, characterized in that the particulate filler consists of inert inorganic particles with particle size smaller than 20,000 nm or of organic or inorganic, natural or

synthetic polymers with a crystalline or amorphous, crosslinked network, of molecular weight between 5000 and 5,000,000.

11. Cosmetic composition according to claim 9, characterized in that the particulate filler consists of organic or inorganic particles of lamellar structure, smaller than 50,000 nm in size.

12. Cosmetic composition according to any one of claims 1 to 11, characterized in that it is in the form of a lotion, thickened lotion, gel, vesicular dispersion, dispersion of nanoparticles, cream, milk, powder, ointment, solid stick, foam or spray.

13. Cosmetic composition according to claim 12, characterized in that it additionally contains cosmetic adjuvants chosen from fatty substances, organic solvents, silicones, thickeners, emollients, UV-A, UV-B or broad band sunscreens, antifoam agents, hydrating agents, perfumes, stabilizers, surfactants, fillers, sequestrants, anionic, cationic, nonionic or amphoteric polymers or mixtures thereof, propellants, alkalifying or acidifying agents, dyes and metal oxide pigments.

14. Cosmetic composition according to any one of claims 1 to 13, constituting a composition protecting the human epidermis against free radicals, characterized in that it is in the form of suspension or dispersion in solvents or fatty substances, the form of emulsion, of cream or milk, the form of ointment, the form of gel, the form of solid stick or of aerosol foam.

15. Cosmetic composition according to any one of claims 1 to 13, employed for the protection of hair against free radicals, characterized in that it is in the form of shampoo, lotion, rinsing gel or composition, to be applied before or after shampooing, before or after dyeing or bleaching, before, during or after permanent waving or straightening, the form of styling or treating lotion or gel, of lotion or gel for blow drying or setting, of hair lacquer, or of permanent waving or hair straightening, dyeing or bleaching composition.

16. Cosmetic composition according to any one of claims 1 to 13, constituting a make-up product for the eyelashes, the eyebrows or the skin, characterized in that it is in the form of treatment cream for the epidermis, make-up foundation, lipstick, eyeshadow, cheek blush, eyeliner or mascara and is in anhydrous or aqueous, solid or pasty form.

17. Cosmetic composition according to any one of claims 1 to 13, constituting a make-up product for hair, characterized in that it is in anhydrous or aqueous, solid or pasty form, the form of water-in-oil or oil-in-water emulsion or the form of a suspension or of a gel.

18. Cosmetic composition according to any one of claims 1 to 13, constituting a product for oral-dental care use, characterized in that it additionally comprises at least one moistening agent, a polishing agent, an active agent or a sweetener.

19. Method for protecting the human epidermis, the mucosae and the hair against free radicals, characterized in that it consists in applying to the latter an effective quantity of a cosmetic composition according to any one of claims 1 to 18.

20. Method for protecting cosmetic compositions against free radicals, characterized in that an effective quantity of the tocopherol/melaninlike pigment combination according to one of claims 1 to 18 is incorporated in the cosmetic compositions.

21. Method for making up the skin, its apparent superficial growths or hair, characterized in that a composition according to one of claims 1 to 17 is applied to them.

AUSTRALIAN PATENT OFFICE

INTERNATIONAL SEARCH REPORT

International application No.
PCT/FR 93/00207

A. CLASSIFICATION OF SUBJECT MATTER

Int.Cl.5 A61K7/42; A61K7/48; A61K7/13

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)

Int.Cl.5 A61K

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

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	FR,A,2 666 226 (THOREL J.N.) 6 March 1992 see page 5, line 4 - line 21 see page 6 - page 7; example 1	1-21
Y	US,A,4 144 325 (VOYT W.F) 13 March 1979 see abstract see column 15; example 6	1-21
Y	EP,A,0 467 767 (L'OREAL) 22 January 1992 cited in the application see page 5, line 17 - line 21	1-21
Y	GB,A,2 207 153 (L'OREAL) 25 January 1989 see page 8, line 2 - line 7 & FR,A,2 618 069 cited in the application	1-21

-/--

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

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

"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
26 April 1993 (26.04.93)	04 June 1993 (04.06.93)
Name and mailing address of the ISA/ European Patent Office Facsimile No.	Authorized officer Telephone No.

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/FR 93/00207

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	EP,A,0 456 545 (L'OREAL) 13 November 1991 see page 3, line 56 - page 4, line 3 ---	1-21
A	EP,A,0 376 776 (L'OREAL) 4 July 1990 cited in the application see the whole document -----	1-21

ANNEX TO THE INTERNATIONAL SEARCH REPORT ON INTERNATIONAL PATENT APPLICATION NO.

FR 9300207
SA 71065

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information. 26/04/93

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
FR-A-2666226	06-03-92	None		
US-A-4144325	13-03-79	US-A-	4975272	04-12-90
EP-A-0467767	22-01-92	FR-A-	2664498	17-01-92
		CA-A-	2047137	17-01-92
		JP-A-	4230305	19-08-92
GB-A-2207153	25-01-89	LU-A-	86946	08-03-89
		BE-A-	1002133	24-07-90
		CA-A-	1301069	19-05-92
		CH-A-	676243	28-12-90
		DE-A-	3824094	26-01-89
		FR-A-	2618069	20-01-89
		JP-A-	1092273	11-04-89
		NL-A-	8801810	16-02-89
		US-A-	4961754	09-10-90
EP-A-0456545	13-11-91	FR-A-	2661673	08-11-91
		AU-A-	7622091	07-11-91
		JP-A-	4225913	14-08-92
EP-A-0376776	04-07-90	LU-A-	87403	10-07-90
		CA-A-	2004742	06-06-90
		JP-A-	2259174	19-10-90
		US-A-	5053053	01-10-91

EPO FORM P0479

RAPPORT DE RECHERCHE INTERNATIONALE

Demande Internationale No PCT/FR 93/00207

I. CLASSEMENT DE L'INVENTION (si plusieurs symboles de classification sont applicables, les indiquer tous) [7]

Selon la classification internationale des brevets (CIB) ou à la fois selon la classification nationale et la CIB

CIB 5 A61K7/42; A61K7/48; A61K7/13

II. DOMAINES SUR LESQUELS LA RECHERCHE A PORTE

Documentation minimale consultée[8]

Système de classification	Symboles de classification
CIB 5	A61K

Documentation consultée autre que la documentation minimale dans la mesure où de tels documents font partie des domaines sur lesquels la recherche a porté[9]

III. DOCUMENTS CONSIDERES COMME PERTINENTS[10]

Catégorie °	Identification des documents cités, avec indication, si nécessaire,[12] des passages pertinents [13]	No. des revendications visées [14]
X,P	FR,A,2 666 226 (THOREL J. N.) 6 Mars 1992 voir page 5, ligne 4 - ligne 21 voir page 6 - page 7; exemple 1 ---	1-21
Y	US,A,4 144 325 (VOYT W.F) 13 Mars 1979 voir abrégé voir colonne 15; exemple 6 ---	1-21
Y	EP,A,0 467 767 (L'OREAL) 22 Janvier 1992 cité dans la demande voir page 5, ligne 17 - ligne 21 --- -/--	1-21

° Catégories spéciales de documents cités:[11]

"A" document définissant l'état général de la technique, non considéré comme particulièrement pertinent

"E" document antérieur, mais publié à la date de dépôt international ou après cette date

"L" document pouvant jeter un doute sur une revendication de priorité ou cité pour déterminer la date de publication d'une autre citation ou pour une raison spéciale (telle qu'indiquée)

"O" document se référant à une divulgation orale, à un usage, à une exposition ou tous autres moyens

"P" document publié avant la date de dépôt international, mais postérieurement à la date de priorité revendiquée

"T" document ultérieur publié postérieurement à la date de dépôt international ou à la date de priorité et n'appartenant pas à l'état de la technique pertinent, mais cité pour comprendre le principe ou la théorie constituant la base de l'invention

"X" document particulièrement pertinent; l'invention revendiquée ne peut être considérée comme nouvelle ou comme impliquant une activité inventive

"Y" document particulièrement pertinent; l'invention revendiquée ne peut être considérée comme impliquant une activité inventive lorsque le document est associé à un ou plusieurs autres documents de même nature, cette combinaison étant évidente pour une personne du métier.

"&" document qui fait partie de la même famille de brevets

IV. CERTIFICATION

1

Date à laquelle la recherche internationale a été effectivement achevée	Date d'expédition du présent rapport de recherche internationale
26 AVRIL 1993	04. 05. 93
Administration chargée de la recherche internationale	**Signature du fonctionnaire autorisé**
OFFICE EUROPEEN DES BREVETS	AVEDIKIAN P.F.

III. DOCUMENTS CONSIDERES COMME PERTINENTS [14] (SUITE DES RENSEIGNEMENTS INDIQUES SUR LA DEUXIEME FEUILLE)

Catégorie °	Identification des documents cités, [16] avec indication, si nécessaire des passages pertinents [17]	No. des revendications visées [18]
Y	GB,A,2 207 153 (L'OREAL) 25 Janvier 1989 voir page 8, ligne 2 - ligne 7 & FR,A,2 618 069 cité dans la demande	1-21
Y	EP,A,0 456 545 (L'OREAL) 13 Novembre 1991 voir page 3, ligne 56 - page 4, ligne 3	1-21
A	EP,A,0 376 776 (L'OREAL) 4 Juillet 1990 cité dans la demande voir le document en entier	1-21

ANNEXE AU RAPPORT DE RECHERCHE INTERNATIONALE RELATIF A LA DEMANDE INTERNATIONALE NO.

FR 9300207
SA 71065

La présente annexe indique les membres de la famille de brevets relatifs aux documents brevets cités dans le rapport de recherche internationale visé ci-dessus.
Lesdits membres sont contenus au fichier informatique de l'Office européen des brevets à la date du
Les renseignements fournis sont donnés à titre indicatif et n'engagent pas la responsabilité de l'Office européen des brevets. 26/04/93

Document brevet cité au rapport de recherche	Date de publication	Membre(s) de la famille de brevet(s)		Date de publication
FR-A-2666226	06-03-92	Aucun		
US-A-4144325	13-03-79	US-A-	4975272	04-12-90
EP-A-0467767	22-01-92	FR-A-	2664498	17-01-92
		CA-A-	2047137	17-01-92
		JP-A-	4230305	19-08-92
GB-A-2207153	25-01-89	LU-A-	86946	08-03-89
		BE-A-	1002133	24-07-90
		CA-A-	1301069	19-05-92
		CH-A-	676243	28-12-90
		DE-A-	3824094	26-01-89
		FR-A-	2618069	20-01-89
		JP-A-	1092273	11-04-89
		NL-A-	8801810	16-02-89
		US-A-	4961754	09-10-90
EP-A-0456545	13-11-91	FR-A-	2661673	08-11-91
		AU-A-	7622091	07-11-91
		JP-A-	4225913	14-08-92
EP-A-0376776	04-07-90	LU-A-	87403	10-07-90
		CA-A-	2004742	06-06-90
		JP-A-	2259174	19-10-90
		US-A-	5053053	01-10-91

EPO FORM P0472