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(54) **COMPOSITION CONTAINING AT LEAST ONE OXIDATION-SENSITIVE HYDROPHILIC ACTIVE PRINCIPLE AND AT LEAST ONE N-VINYLMIDAZOLE POLYMER OR COPOLYMER USEFUL TO PREVENT AND/OR TREAT CUTANEOUS SIGNS OF INTRINSIC AGEING**

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(57) **ABSTRACT**

The invention relates to a composition containing, preferably in a physiologically acceptable medium comprising an aqueous phase, at least one oxidation-sensitive hydrophilic active principle selected from the group consisting of ascorbic acid and its derivatives and at least one non-crosslinked N-vinylimidazole polymer or copolymer, the active principle and the polymer or copolymer both being in the aqueous phase, useful for preventing and/or treating cutaneous signs of intrinsic ageing.

**COMPOSITION CONTAINING AT LEAST ONE
OXIDATION-SENSITIVE HYDROPHILIC ACTIVE
PRINCIPLE AND AT LEAST ONE
N-VINYLMIDAZOLE POLYMER OR
COPOLYMER USEFUL TO PREVENT AND/OR
TREAT CUTANEOUS SIGNS OF INTRINSIC
AGEING**

FIELD OF THE INVENTION

[0001] The present invention relates to a composition comprising at least one oxidation-sensitive hydrophilic active principle and at least one N-vinylimidazole polymer or copolymer in a physiologically acceptable medium comprising an aqueous phase, and its use in particular to prevent or treat cutaneous signs of intrinsic ageing. The composition is preferably a cosmetic or dermatological composition.

BACKGROUND OF THE INVENTION

[0002] It is known to introduce, into cosmetic compositions, various active principles intended to contribute specific treatments to the skin and/or hair. However, some of these active principles exhibit the disadvantage of being unstable in an aqueous medium and of easily decomposing on contact with water, in particular because of oxidation phenomena. They thus rapidly lose their activity over time and this instability conflicts with the desired effectiveness.

[0003] Attempts have thus been made for a long time to formulate ascorbic acid or vitamin C because of its numerous beneficial properties. In particular, ascorbic acid stimulates the synthesis of the connective tissue and in particular of collagen, strengthens the defences of the cutaneous tissue against external attacks, such as ultraviolet radiation and pollution, compensates for vitamin E deficiency of the skin, depigments the skin and has a role in combating free radicals. These last two properties make it an excellent candidate as cosmetic or dermatological active principle for combating ageing of the skin or for preventing ageing of the skin. Unfortunately, because of its chemical structure (of α -ketolactone), ascorbic acid is highly sensitive to certain environmental parameters and in particular to oxidation phenomena. There thus ensues rapid decomposition of formulated ascorbic acid in the presence of these parameters and in particular in the presence of oxygen, light or metal ions, as a function of the temperature or under certain pH conditions (Pharm. Acta. Helv., 1969, 44, 611-667; STP Pharma, 1985, 4, 281-286).

[0004] Several solutions have thus been envisaged in the prior art for reducing and/or slowing down the decomposition of ascorbic acid.

[0005] Provision has thus been made to use ascorbic acid in the form of a chemical derivative (magnesium ascorbyl phosphate or esters of fatty acids and ascorbic acid), but the bioavailability of these derivatives is very low (J. Am. Acad. Dermatol., 1996, 34, 29-33).

[0006] The instability of ascorbic acid with respect to oxygen can be improved by using specific packagings, such as twin compartments under an inert atmosphere, as disclosed in U.S. Pat. No. 5,935,584, or alternatively by the use of two-phase emulsions, one phase of which is composed of a dry powder comprising ascorbic acid and the second phase of which is a liquid phase. The mixing of the two phases has

to be carried out at the time of use (WO 98/43598). These solutions have disadvantages with regard to the cost and the complexity of the manufacturing operations and significant restrictions with regard to use.

[0007] Another solution provided in the prior art consists in using a high concentration of glycols or polyols in order to reduce the solubility of oxygen in the formulation, thus protecting the ascorbic acid (WO 96/24325, EP 0 755 674, U.S. Pat. No. 5,981,578). The polyols can optionally be incorporated in liposomes, as disclosed in U.S. Pat. No. 6,020,367. However, these solutions exhibit the disadvantage of resulting in sticky formulations, the cosmetic quality of which is difficult to improve. Furthermore, the presence of a high concentration of these compounds can lead to phenomena of irritation.

[0008] Ascorbic acid can also be formulated in anhydrous media, such as silicones (U.S. Pat. No. 6,194,452), which are capable of creating an anhydrous barrier around ascorbic acid. A major disadvantage of such solutions results from the lack of freshness on application.

[0009] The need thus remains for a composition employable in particular in the cosmetics field, in which a hydrophilic active principle which is unstable in an oxidizing medium is stabilized, which is comfortable on application, which does not lead to any skin irritation after application and which is compatible with the constraints of an industrial implementation of its manufacturing process.

[0010] The effect of ascorbic acid on the biosynthesis of collagen, a protein macromolecule predominantly present in the dermis, has been known for several years (Arch. Biochem. Biophys., 152, 1972, p. 318-328). It acts at two levels. First of all, as cofactor of hydroxylases, enzymes involved in the hydroxylation of proline and of lysine, ascorbic acid promotes this essential stage in the assembling of procollagen molecules (Biochemistry, 78(5), 1981, p. 2279-2282; The Yale Journal of Biology and Medicine, 58, 1985, p. 553-559). Furthermore, it stimulates the biosynthesis of collagen by increasing the amount of mRNA coding for procollagens of type I and III (The Journal of Investive Dermatology, 90(4), 1988, p. 420-424).

[0011] Magnesium ascorbyl phosphate also stimulates the synthesis of collagen (Skin Pharmacol., 6, 1993, p. 65-71).

[0012] At the same time as these properties, the ascorbic acid used to treat cutaneous fibroblasts has made it possible to demonstrate an increase in proteoglycans (Journal of Biochemical Engineering, 1991, 113).

[0013] More recently, it has been shown that magnesium ascorbyl phosphate, added to a medium for the culturing of reconstructed skin, led to a significant increase in the number of fibroblasts in the lattice, in combination with significant stimulation of the synthesis of proteins of the extracellular matrix (FR-02/01510). This was observed in particular at the dermoepidermal junction, where stimulation of the synthesis of the major components, which are collagens IV and VII, and laminin, is measured. This phenomenon has the consequence of reinforcing the relief of this junction, promoting exchanges between dermis and epidermis, and the cohesion of these two tissues, and thus makes it possible to combat the harmful effects of ageing on these factors.

[0014] By enhancing the overall content of collagen, the proliferative capability and the synthetic activity of fibro-

blasts and the amount of procollagen I and III, but also by reinforcing the cohesion and the effectiveness of the dermoepidermal junction, ascorbic acid and its derivatives are therefore particularly useful in preventing and/or treating cutaneous signs of intrinsic ageing.

OBJECTS OF THE INVENTION

[0015] One object of the present invention is to provide a composition comprising an oxidation-sensitive active principle for example selected from the group consisting of ascorbic acid and its derivatives, which exhibits good cosmetic properties, both with regard to touch and with regard to tolerance, the preservation of which over time does not require specific precautions, and which retains the activity of the said active principle in the prevention and/or the treatment of cutaneous signs of intrinsic ageing.

DETAILED DESCRIPTION OF THE INVENTION

[0016] The inventors have discovered that the use of non-crosslinked N-vinylimidazole polymers or copolymers in compositions in which the aqueous phase includes an oxidation-sensitive active principle, such as ascorbic acid or one of its derivatives, makes it possible to achieve the abovementioned aim.

[0017] In the prior art, some compounds having an imidazole structure have been disclosed for their stabilizing properties. Thus, in Patent Application EP 0 586 106, several imidazole-based molecules are used to stabilize certain retinoids against chemical decomposition. Furthermore, polymeric emulsifiers composed of N-vinylimidazole, of alkyl acrylates and of vinyl acetates are disclosed in U.S. Pat. No. 4,057,622. They are used for the purpose of replacing known emulsifiers in order to overcome their disadvantages, in particular with regard to smell, and to stabilize water-in-oil emulsions. Finally, N-vinylimidazole/N-vinylcaprolactam/N-vinylpyrrolidone copolymers are disclosed in U.S. Pat. No. 6,191,188. They are used in the manufacture of hair-strengthening compositions.

[0018] To the knowledge of the inventors, polymers or copolymers comprising N-vinylimidazole units have never been used in combination with hydrophilic active principles sensitive to decomposition by oxidation for the purpose of improving their stability in an aqueous medium. This is true in particular in the case of ascorbic acid.

[0019] One embodiment of the present invention is therefore the preferably cosmetic and/or dermatological use, for preventing and/or treating cutaneous signs of intrinsic ageing, of a composition comprising, in a physiologically acceptable medium comprising an aqueous phase, at least one oxidation-sensitive hydrophilic active principle preferably selected from the group consisting of ascorbic acid and its derivatives and at least one non-crosslinked N-vinylimidazole polymer or copolymer, the active principle and the polymer or copolymer both being in the aqueous phase. The copolymer is preferably present in an amount sufficient to stabilize the said oxidation-sensitive hydrophilic active principle, and the composition is preferably applied to those areas of the skin in need of such prevention and/or treatment.

[0020] Another embodiment of the invention is the use of a combination composed of at least one oxidation-sensitive

hydrophilic active principle preferably selected from the group consisting of ascorbic acid and its derivatives and of at least one non-crosslinked N-vinylimidazole polymer or copolymer in the aqueous phase of a cosmetic composition as agent for preventing and/or treating cutaneous signs of intrinsic ageing.

[0021] According to the invention, the term "intrinsic ageing" is understood to mean the ageing which occurs because of modifications due to endogenous factors, in contrast to ageing caused by exogenous factors, such as photoageing. The changes in the skin which occur are then revealed for example by a thinning of the dermis, a loss of elasticity, a deepening of the imperfections and the appearance of fine lines.

[0022] According to the invention, the term "hydrophilic active principle" is understood to mean a compound having a solubility in water of at least 0.25% at ambient temperature (25° C.).

[0023] According to the invention, the term "oxidation-sensitive hydrophilic active principle" is understood to mean any active principle of natural or synthetic origin capable of undergoing decomposition by an oxidation mechanism. This oxidation phenomenon can have several causes, in particular the presence of oxygen, of light or of metal ions, a high temperature or certain pH conditions.

[0024] Mention may be made, by way of example and without implied limitation, of: ascorbic acid and its derivatives, such as salts and esters thereof, particularly the 5,6-di-O-dimethylsilylascorbate (sold by Exsymol under the reference PRO-AA), the potassium salt of dl- α -tocopheryl dl-ascorbyl phosphate (sold by Senju Pharmaceutical under the reference SEPIVITAL EPC), magnesium ascorbyl phosphate or sodium ascorbyl phosphate (sold by Roche under the reference Stay-C 50). The principle is preferably present in an amount sufficient to prevent and/or treat cutaneous signs of ageing, such as 0.1, 1, 5 and 25 g per 100 g. Any principle useful for this purpose and meeting the requirements of hydrophilicity and oxidation sensitivity may be used.

[0025] In a particularly advantageous aspect, the oxidation-sensitive hydrophilic active principle is ascorbic acid.

[0026] According to the invention, the term "non-crosslinked N-vinylimidazole polymer or copolymer" is understood to mean any polymer comprising N-vinylimidazole units and not comprising a crosslinking agent. Copolymers suitable for the implementation of the invention are copolymers combining N-vinylimidazole with N-vinylpyrrolidone and/or N-vinylcaprolactam subunits.

[0027] In an advantageous aspect of the invention, the copolymer has a molar fraction of N-vinylimidazole units of between 0.1 and 1, more preferably between 0.4 and 0.9, inclusive.

[0028] According to an advantageous aspect of the invention, the molar ratio of the N-vinylimidazole unit equivalent to the oxidation-sensitive hydrophilic active principle varies between 0.004 and 16 and preferably between 0.01 and 1, inclusive.

[0029] Use will preferably be made of an N-vinylimidazole/N-vinylpyrrolidone copolymer.

[0030] The weight-average molar mass of the N-vinylimidazole polymers will advantageously be between 1 000 and 1×10^7 and preferably between 5 000 and 5×10^6 .

[0031] Use may be made, to this end, of the vinylpyrrolidone/vinylimidazole (50/50) copolymer having a weight-average molar mass of 1 200 000 sold under the reference LUVITEC VPI 55K72W by BASF or the vinylpyrrolidone/vinylimidazole (50/50) copolymer having a weight-average molar mass of 10 000 sold under the reference LUVITEC VPI 55K18P by BASF.

[0032] The at least one polymer or copolymer is preferably present in the composition according to the invention in an amount sufficient to produce the desired effect, that is to say in an amount sufficient to stabilize the oxidation-sensitive hydrophilic active principle. Preferably, the copolymer is present at a concentration of between 0.1 and 5% by weight with respect to the total weight of the aqueous phase and more particularly at a concentration of between 0.1 and 2% by weight with respect to the total weight of the aqueous phase, inclusive. Preferably the amount stabilizes the active principle by slowing or stopping decomposition at 45° C. for two months.

[0033] The compositions used according to the invention are preferably intended for topical application to the skin and/or its superficial body growths and therefore comprise a physiologically acceptable medium, that is to say a medium compatible with cutaneous tissues, such as the skin, scalp, eyelashes, eyebrows, hair, nails and mucous membranes. This physiologically acceptable medium comprises an aqueous phase and optionally a physiologically acceptable organic solvent chosen, for example, from lower alcohols comprising from 1 to 8 carbon atoms and in particular from 1 to 6 carbon atoms, such as ethanol, isopropanol, propanol or butanol; polyethylene glycols having from 6 to 80 ethylene oxide units; or polyols, such as propylene glycol, isoprene glycol, butylene glycol, glycerol or sorbitol.

[0034] When the physiologically acceptable medium is an aqueous medium, it generally preferably has a pH which is compatible with the skin, preferably ranging from 3 to 9 and better still from 3.5 to 7.5.

[0035] The compositions according to the invention can be provided in any form, including any pharmaceutical dosage form used for topical application and in particular in the form of aqueous or aqueous/alcoholic solutions, of oil-in-water (O/W) or water-in-oil (W/O) or multiple (triple: W/O/W or O/W/O) emulsions, of aqueous gels or of dispersions of a fatty phase in an aqueous phase using spherules, it being possible for these spherules to be polymeric nanoparticles, such as nanospheres and nanocapsules, or lipid vesicles of ionic and/or nonionic type (liposomes, niosomes or oleosomes). These compositions are prepared according to the usual methods.

[0036] In addition, the compositions used according to the invention can be more or less fluid and can have the appearance of a white or coloured cream, of an ointment, of a milk, of a lotion, of a serum, of a paste or of a foam. They can optionally be applied to the skin in the form of an aerosol. They can also be provided in a solid form, for example in the form of a stick.

[0037] When the composition used according to the invention comprises an oily phase, the latter preferably comprises at least one oil. It can additionally comprise other fatty substances.

[0038] Mention may be made, as oils which can be used in the composition of the invention, of, for example:

[0039] hydrocarbonaceous oils of animal origin, such as perhydrosqualene;

[0040] hydrocarbonaceous oils of vegetable origin, such as liquid triglycerides of fatty acids comprising from 4 to 10 carbon atoms, such as triglycerides of heptanoic acid or octanoic acid, or alternatively, for example, sunflower, maize, soybean, gourd, grape seed, sesame, hazelnut, apricot, macadamia, arara, castor or avocado oils, triglycerides of caprylic/capric acids, such as those sold by Stéarineries Dubois or those sold under the names Miglyol 810, 812 and 818 by Dynamit Nobel, jojoba oil, or karite butter oil;

[0041] synthetic esters and ethers, in particular of fatty acids, such as the oils of formulae R1COOR2 and R1OR2 in which R1 represents the residue of a fatty acid comprising from 8 to 29 carbon atoms and R2 represents a branched or unbranched hydrocarbonaceous chain comprising from 3 to 30 carbon atoms, such as, for example, purcellin oil, isononyl isononanoate, isopropyl myristate, 2-ethylhexyl palmitate, 2-octyldodecyl stearate, 2-octyldodecyl erucate or isostearyl isostearate; hydroxylated esters, such as isostearyl lactate, octyl hydroxystearate, octyldodecyl hydroxystearate, diisostearyl malate, triisocetyl citrate or heptanoates, octanoates or decanoates of fatty alcohols; polyol esters, such as propylene glycol dioctanoate, neopentyl glycol diheptanoate and diethylene glycol diisononanoate; and pentaerythritol esters, such as pentaerythrityl tetraistearate;

[0042] linear or branched hydrocarbons of mineral or synthetic origin, such as volatile or nonvolatile liquid paraffins and their derivatives, liquid petrolatum, polydecenes or hydrogenated polyisobutene, such as parleam oil;

[0043] fatty alcohols having from 8 to 26 carbon atoms, such as cetyl alcohol, stearyl alcohol and their mixture (cetearyl alcohol), octyldodecanol, 2-butyl-octanol, 2-hexyldecanol, 2-undecylpentadecanol, oleyl alcohol or linoleyl alcohol;

[0044] partially hydrocarbon-comprising and/or silicone-comprising fluorinated oils, such as those disclosed in the document JP-A-2-295912;

[0045] silicone oils, such as volatile or nonvolatile polymethylsiloxanes (PDMS) comprising a linear or cyclic silicone chain which are liquid or pasty at ambient temperature, in particular cyclopolydimethylsiloxanes (cyclomethicones), such as cyclohexasiloxane; polydimethylsiloxanes comprising pendent alkyl, alkoxy or phenyl groups or alkyl, alkoxy or phenyl groups at the end of the silicone chain, which groups have from 2 to 24 carbon atoms; or phenylated silicones, such as phenyl trimethicones, phenyl

dimethicones, phenyltrimethylsiloxydiphenylsiloxanes, diphenyl dimethicones, diphenylmethyl-diphenyltrisiloxanes, (2-phenylethyl)trimethylsiloxy-silicates and polymethylphenylsiloxanes;

[0046] their mixtures.

[0047] The term "hydrocarbonaceous oil" is understood to mean, in the list of the oils mentioned above, any oil predominantly comprising carbon and hydrogen atoms and optionally ester, ether, fluorinated, carboxylic acid and/or alcohol groups.

[0048] The other fatty substances which can be present in the oily phase are, for example, fatty acids comprising from 8 to 30 carbon atoms, such as stearic acid, lauric acid, palmitic acid and oleic acid; waxes, such as lanolin, beeswax, carnauba or candelilla wax, paraffin or lignite waxes or microcrystalline waxes, ceresin or ozokerite, or synthetic waxes, such as polyethylene waxes or Fischer-Tropsch waxes; silicone resins, such as trifluoromethyl C1-4 alkyl dimethicone and trifluoropropyl dimethicone; and silicone elastomers, such as the products sold under the names "KSG" by Shin-Etsu, under the names "Trefil", "BY29" or "EPSX" by Dow Corning or under the names "Gransil" by Grant Industries.

[0049] These fatty substances can be chosen in a way varied by a person skilled in the art in order to prepare a composition having the desired properties, for example of consistency or of texture, without undue hardship.

[0050] According to a specific embodiment of the invention, the composition according to the invention is a water-in-oil (W/O) or oil-in-water (O/W) emulsion. The proportion of the oily phase in the emulsion can preferably range from 5 to 80% by weight and preferably from 5 to 50% by weight with respect to the total weight of the composition.

[0051] The emulsions generally comprise at least one emulsifier selected from the group consisting of amphoteric, anionic, cationic or nonionic emulsifiers, used alone or as a mixture, and optionally a coemulsifier. The emulsifiers are appropriately chosen according to the emulsion to be obtained (W/O or O/W). The emulsifier and the coemulsifier are generally present in the composition in a proportion ranging from 0.3 to 30% by weight and preferably from 0.5 to 20% by weight with respect to the total weight of the composition.

[0052] Mention may be made, for the W/O emulsions, for example, as emulsifiers, of dimethicone copolyols, such as the mixture of cyclomethicone and of dimethicone copolyol sold under the name "DC 5225 C" by Dow Corning, and alkyl dimethicone copolyols, such as the laurylmethicone copolyol sold under the name "Dow Corning 5200 Formulation Aid" by Dow Corning and the cetyl dimethicone copolyol sold under the name Abil EM 90R by Goldschmidt. Use may also be made, as surfactant of W/O emulsions, of a crosslinked solid organopolysiloxane elastomer comprising at least one oxyalkylenated group, such as those obtained according to the procedure of Examples 3, 4 and 8 of the document U.S. Pat. No. 5,412,004 and the examples of the document U.S. Pat. No. 5,811,487, in particular the product of Example 3 (synthetic example) of patent U.S. Pat. No. 5,412,004, and such as that sold under the reference KSG 21 by Shin Etsu. Use may also be made, as emulsifier, of a polyolefin-derived oligomer or polymer comprising a suc-

cinic ending; the latter is preferably a polyolefin comprising an esterified or amidated succinic ending or a salt of such a polyolefin and in particular polyisobutylene comprising an esterified or amidated succinic ending such as the products sold under the names L5603 and L2721 and OS131769 by Lubrizol.

[0053] Mention may be made, for the O/W emulsions, for example, as emulsifiers, of nonionic emulsifiers, such as esters of fatty acids and of glycerol which are oxyalkylenated (more particularly polyoxyethylenated); esters of fatty acids and of sorbitan which are oxyalkylenated; esters of fatty acids which are oxyalkylenated (oxyethylenated and/or oxypropylenated); ethers of fatty alcohols which are oxyethylenated (oxyethylenated and/or oxypropylenated); sugar esters, such as sucrose stearate; and their mixtures, such as the mixture of glyceryl stearate and of PEG-40 stearate.

[0054] The composition of the invention can also comprise adjuvants known in the cosmetics or dermatological field, such as hydrophilic or lipophilic gelling agents, preservatives, solvents, fragrances, fillers, UV screening agents, bactericides, odour absorbers, colouring materials, plant extracts or salts. The amounts of these various adjuvants are those conventionally used in the field under consideration, for example from 0.01 to 20% of the total weight of the composition. These adjuvants, depending on their nature, can be introduced into the fatty phase, into the aqueous phase and/or into the lipid spherules.

[0055] Mention may be made, as fillers which can be used in the composition of the invention, for example, of pigments, silica powder; talc; particles of polyamide and in particular those sold under the name Orgasol by Atochem; polyethylene powders; microspheres based on acrylic copolymers, such as those made of ethylene glycol dimethacrylate/lauryl methacrylate copolymer which are sold by Dow Corning under the name Polytrap; expanded powders, such as hollow microspheres and in particular the microspheres sold under the name Expancel by Kernard Plast or under the name Micropearl F 80 ED by Matsumoto; silicone resin microbeads, such as those sold under the name Tospearl by Toshiba Silicone; and their mixtures. These fillers can be present in amounts ranging from 0 to 20% by weight and preferably from 1 to 10% by weight with respect to the total weight of the composition.

[0056] According to a preferred embodiment, the compositions in accordance with the invention can additionally comprise at least one organic photoprotective agent and/or at least one inorganic photoprotective agent which is active in the UV-A and/or UV-B regions (absorbers), and which are soluble in water or in fats or else are insoluble in the cosmetic solvents commonly used.

[0057] The organic photoprotective agents are chosen in particular from anthranilates; cinnamic derivatives; dibenzoylmethane derivatives; salicylic derivatives; camphor derivatives; triazine derivatives, such as those disclosed in patent applications U.S. Pat. No. 4,367,390, EP 863 145, EP 517 104, EP 570 838, EP 796 851, EP 775 698, EP 878 469, EP 933 376, EP 507 691, EP 507 692, EP 790 243 and EP 944 624; benzophenone derivatives; β , β -diphenylacrylate derivatives; benzotriazole derivatives; benzalmonate derivatives; benzimidazole derivatives; imidazolines; bisbenzoozoyl derivatives as disclosed in Patents EP 669 323 and U.S. Pat. No. 2,463,264; p-aminobenzoic acid (PABA)

derivatives; methylenebis(hydroxyphenylbenzotriazole) derivatives as disclosed in applications U.S. Pat. No. 5,237,071, U.S. Pat. No. 5,166,355, GB 2 303 549, DE 197 26 184 and EP 893 119; screening polymers and screening silicones, such as those disclosed in particular in Application WO 93/04665; dimers derived from α -alkylstyrene, such as those disclosed in Patent Application DE 198 55 649; 4,4-diarylbutadienes as disclosed in Applications EP 0 967 200, DE 197 46 654, DE 197 55 649, EP-A-1 008 586, EP 1 133 980 and EP 133 981; and their mixtures.

[0058] By way of illustration, mention may be made, as photoprotective agents which are active in the UV-A and/or UV-B regions, denoted below under their INCI names, of:

[0059] p-aminobenzoic acid (PABA) derivatives, in particular PABA, ethyl PABA, ethyl dihydroxypropyl PABA, ethylhexyl dimethyl PABA (sold in particular under the name "Escalol 507" by ISP), glyceryl PABA or PEG-25 PABA (sold under the name "Uvinul P25" by BASF),

[0060] salicylic derivatives, in particular homosalate (sold under the name "Eusolex HMS" by Rona/EM Industries), ethylhexyl salicylate (sold under the name "Neo Heliopan OS" by Haarmann and Reimer), dipropylene glycol salicylate (sold under the name "Dipsal" by Scher), or TEA salicylate (sold under the name "Neo Heliopan TS" by Haarmann and Reimer),

[0061] dibenzoylmethane derivatives, in particular butyl methoxydibenzoylmethane (sold in particular under the trade name "Parsol 1789" by Hoffmann-LaRoche), or isopropyl dibenzoylmethane,

[0062] cinnamic derivatives, in particular ethylhexyl methoxycinnamate (sold in particular under the trade name "Parsol MCX" by Hoffmann-LaRoche), isopropyl methoxycinnamate, isoamyl methoxycinnamate (sold under the trade name "Neo Heliopan E 1000" by Haarmann and Reimer), cinoxate, DEA methoxycinnamate, diisopropyl methyl cinnamate, or glyceryl ethylhexanoate dimethoxycinnamate,

[0063] β,β -diphenylacrylate derivatives, in particular octocrylene (sold in particular under the trade name "Uvinul N539" by BASF) or etocrylene (sold in particular under the trade name "Uvinul N35" by BASF),

[0064] benzophenone, in particular benzophenone-1 (sold under the trade name "Uvinul 400" by BASF), benzophenone-2 (sold under the trade name "Uvinul D50" by BASF), benzophenone-3 or oxybenzone (sold under the trade name "Uvinul M40" by BASF), benzophenone-4 (sold under the trade name "Uvinul MS40" by BASF), benzophenone-5, benzophenone-6 (sold under the trade name "Helisorb 11" by Norquay), benzophenone-8 (sold under the trade name "Spectra-Sorb UV-24" by American Cyanamid), benzophenone-9 (sold under the trade name "Uvinul DS-49" by BASF), benzophenone-12, or n-hexyl 2-(4-diethylamino-2-hydroxybenzoyl)benzoate,

[0065] benzylidene camphor derivatives, in particular 3-benzylidene camphor (manufactured under the

name "Mexoryl SD" by Chimex), 4-methylbenzylidene camphor (sold under the name "Eusolex 6300" by Merck), benzylidene camphor sulphonic acid (manufactured under the name "Mexoryl SL" by Chimex), camphor benzalkonium methosulphate (manufactured under the name "Mexoryl SO" by Chimex), terephthalylidene dicamphor sulphonic acid (manufactured under the name "Mexoryl SX" by Chimex), or polyacrylamidomethyl benzylidene camphor (manufactured under the name "Mesoryl SW" by Chimex),

[0066] benzimidazole derivatives, in particular phenylbenzimidazole sulphonic acid (sold in particular under the trade name "Eusolex 232" by Merck), or disodium phenyl dibenzimidazole tetrasulphonate (sold under the trade name "Neo Heliopan AP" by Haarmann and Reimer),

[0067] triazine derivatives, in particular anisotriazine (sold under the trade name "Tinosorb S" by Ciba Specialty Chemicals), ethylhexyl triazone (sold in particular under the trade name "Uvinul T150" by BASF), diethylhexyl butamido triazone (sold under the trade name "Uvasorb HEB" by Sigma 3V) or 2,4,6-tris(diisobutyl 4'-amino-benzalmonate)-s-triazine,

[0068] benzotriazole derivatives, in particular drometrisole trisiloxane (sold under the name "Silatriazole" by Rhodia Chimie) or methylene bisbenzotriazolyl tetramethylbutylphenol (sold in the solid form under the trade name "Mixxim BB/100" by Fairmount Chemical or in the micronized form in aqueous dispersion under the trade name "Tinosorb M" by Ciba Specialty Chemicals),

[0069] anthranilic derivatives, in particular menthyl anthranilate (sold under the trade name "Neo Heliopan MA" by Haarmann and Reimer),

[0070] imidazoline derivatives, in particular ethylhexyl dimethoxybenzylidene dioxoimidazoline propionate,

[0071] benzalmonate derivatives, in particular polyorganosiloxane comprising benzalmonate functional groups (sold under the trade name "Parsol SLX" by Hoffmann-LaRoche),

[0072] 4,4-diarylbutadiene derivatives, in particular 1,1'-dicarboxy (2,2'-dimethyl-propyl)-4,4-diphenylbutadiene,

[0073] and their mixtures.

[0074] The organic photoprotective agents which are more particularly preferred are selected from the group consisting of ethylhexyl salicylate, ethylhexyl methoxycinnamate, octocrylene, phenylbenzimidazole sulphonic acid, benzophenone-3, benzophenone-4, benzophenone-5, 4-methylbenzylidene camphor, terephthalylidene dicamphor sulphonic acid, disodium phenyl dibenzimidazole tetrasulphonate, 2,4,6-tris(diisobutyl 4'-aminobenzalmonate)-s-triazine, anisotriazine, ethylhexyl triazone, diethylhexyl butamido triazone, methylene bisbenzotriazolyl tetramethylbutylphenol, drometrisole trisiloxane, 1,1'-dicarboxy (2,2'-dimethylpropyl)-4,4-diphenylbutadiene, and their mixtures.

[0075] The inorganic photoprotective agents may be selected from the group consisting of pigments or alternatively nanopigments (mean size of the primary particles: generally between 5 nm and 100 nm, preferably between 10 nm and 50 nm) formed from coated or uncoated metal oxides, such as, for example, titanium oxide (amorphous or crystalline in the rutile and/or anatase form), iron oxide, zinc oxide, zirconium oxide or cerium oxide nanopigments, which are all UV photoprotective agents well known per se. Conventional coating agents are, furthermore, alumina and/or aluminium stearate. Such nanopigments formed from coated or uncoated metal oxides are disclosed in particular in Patent Applications EP 518 772 and EP 518 773.

[0076] The photoprotective agents are generally preferably present in the compositions according to the invention in proportions ranging from 0.1 to 20% by weight with respect to the total weight of the composition and preferably ranging from 0.2 to 15% by weight with respect to the total weight of the composition.

[0077] In another advantageous aspect of the invention, the composition can additionally (that is, in addition to the principle described above) comprise at least one other active principle which stimulates dermal macromolecules or which prevents their decomposition and/or one agent which stimulates the proliferation of fibroblasts or keratinocytes and/or the differentiation of keratinocytes.

[0078] Examples include active principles which stimulate dermal macromolecules or which prevent their decomposition, those which act:

[0079] either on the synthesis of collagen, such as extracts of *Centella asiatica*; asiaticosides and derivatives; ascorbic acid or vitamin C and its derivatives, synthetic peptides, such as iamine, bio-peptide CL or the palmitoyl oligopeptide sold by Sederma; peptides extracted from plants, such as the soybean hydrolysate sold by Coletica under the trade name Phytokine®; and plant hormones, such as auxins;

[0080] or on the synthesis of elastin, such as the extract of *Saccharomyces cerevisiae* sold by LSN under the trade name Cytovitin®; and the extract of the alga *Macrocystis pyrifera* sold by Secma under the trade name Kelpadeli®;

[0081] or on the synthesis of glycosaminoglycans, such as the product of fermentation of milk by *Lactobacillus vulgaris* sold by Brooks under the trade name Biomin yogourth®; the extract of the brown alga *Padina pavonica* sold by Alban Müller under the trade name HSP3®; and the extract of *Saccharomyces cerevisiae* available in particular from Silab under the trade name Firmalift® or from LSN under the trade name Cytovitin®;

[0082] or on the synthesis of fibronectin, such as the extract of *Salina zooplankton* sold by Seporga under the trade name GP4G®;

[0083] the yeast extract available in particular from Alban Müller under the trade name Drieline®; and the palmitoyl pentapeptide sold by Sederma under the trade name Matrixil®;

[0084] or on the inhibition of metalloproteinases (MMP), 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 Coletica under the trade name Collalift®; extracts of blueberry or of rosemary; lycopene; or isoflavones, their derivatives or the plant extracts comprising them, in particular extracts of soybean (sold, for example, by Ichimaru Pharcos under the trade name Flavosterone SB®), of red clover, of flax, of kakkon or of sage;

[0085] or on the inhibition of serine proteases, such as leukocyte elastase or cathepsin G. Mention may be made of: the peptide extract of Leguminosae (*Pisum sativum*) seeds sold by LSN under the trade name Parelasyt®; heparinoids; and pseudodipeptides.

[0086] Mention may in particular be made, among the active principles which stimulate epidermal macromolecules, such as filaggrin and keratins, of the extract of lupin sold by Silab under the trade name Structurine®; the extract of beech *Fagus sylvatica* buds sold by Gattefossé under the trade name Gatuline®; and the extract of *Salina zooplankton* sold by Seporga under the trade name GP4G®.

[0087] The agents which stimulate the proliferation of fibroblasts which can be used in the composition according to the invention can, for example, be selected from the group consisting of plant proteins or polypeptides, extracts, in particular of soybean (for example, a soybean extract sold by LSN under the name Eleseryl SH-VEG 8® or sold by Silab under the trade name Raffermine®); and plant hormones, such as gibberellins and cytokinins.

[0088] The agents which stimulate the proliferation of keratinocytes which can be used in the composition according to the invention may comprise in particular retinoids, such as retinol and its esters, including retinyl palmitate; phloroglucinol; the extracts of walnut meal sold by Gattefossé; and the extracts of *Solanum tuberosum* sold by Sederma.

[0089] The agents which stimulate the differentiation of keratinocytes include for example inorganic materials, such as calcium; the extract of lupin sold by Silab under the trade name Photopréventine®; sodium β -sitosteryl sulphate, sold by Seporga under the trade name Phytocohésine®; and the extract of maize sold by Solabia under the trade name Phytovityl®.

[0090] The composition according to the invention can be applied to the skin or mucous membranes. It can thus be used in a cosmetic treatment process for the purpose of preventing and/or treating cutaneous signs of intrinsic ageing, comprising the application of the composition according to the invention to the skin or mucous membranes, particularly skin or membranes especially subject to such ageing and its signs, and more particularly such skin and membranes visible in normal activity.

[0091] In an alternative form, the composition according to the invention can be used for the manufacture of a dermatological preparation comprising an aqueous phase which is intended to prevent and/or treat cutaneous signs of intrinsic ageing.

[0092] The examples which follow serve to illustrate the invention without, however, exhibiting a limiting nature. The compounds are, depending on the situation, cited according to chemical names or according to CTFA (International Cosmetic Ingredient Dictionary and Handbook) names.

EXAMPLES

Example 1

[0093] Accelerated Storage Test.

[0094] The aim of this test is to study the decomposition of an oxidation-sensitive hydrophilic active principle after storing for two months at 45° C. Various solutions were prepared and their compositions are collated in the following table:

TABLE I

Compositions (in water)	Solution A Control	Solution B	Solution C	Solution D
Ascorbic acid	15%	15%	15%	15%
Polymer 1	—	1%	—	—
Polymer 2	—	—	1%	—
Polymer 3	—	—	—	1%

[0095] All the solutions are brought to pH 6 with 8.9 mol/l KOH.

[0096] The percentages of the polymers are given as active material.

[0097] Polymer 1: Vinylpyrrolidone/vinylimidazole (50/50) copolymer sold under the reference Luvitec VPI 55K72W of BASF (Weight-average molecular mass 1.2×10^6).

[0098] Polymer 2: Vinylpyrrolidone/vinylimidazole (50/50) copolymer sold under the reference Luvitec VPI 55K8P of BASF (Weight-average molecular mass 10 000).

[0099] Polymer 3: Polyvinylpyrrolidone sold under the reference Kollidon 12PF of BASF (Weight-average molecular mass 3 000).

[0100] The degree of decomposition measured is given by the ratio:

$$(C0-C2 \text{ months})/C0$$

[0101] with C0 concentration of ascorbic acid at t=0 and C2 months the concentration of ascorbic acid at t=2 months, under the conditions indicated in the above table.

[0102] The concentration of ascorbic acid is determined by the HPLC technique (LaChrom Merck system). The analytical conditions are as follows:

[0103] Column: Lichrosphere100 RP18 (250 mm)

[0104] Eluent: 0.1M phosphate buffer, pH 2.1

[0105] Flow rate: 1 ml/min

[0106] Detection at 257 nm

[0107] Dilution of the sample such that the concentration of ascorbic acid is between 0.05 and 1 mg/ml.

[0108] The results obtained are collated in the following Table II:

TABLE II

	Degree of decomposition after 2 months at 45° C. (in %)	
	under air, amber glass bottle	under nitrogen, aluminium flask
Solution A	43	19.4
Solution B	10.8	1
Solution C	23.4	4.5
Solution D	35.8	15.7

[0109] It is found, from Table II, that the stability of ascorbic acid is improved in the presence of Polymer 1 and Polymer 2 of the invention, even in the presence of atmospheric oxygen, in comparison with the control. It is also found that the N-vinylpyrrolidone homopolymer alone is not sufficient to effectively stabilize the ascorbic acid solution.

[0110] As the polymers mentioned are hydrophilic, it will be sufficient to add them to an aqueous ascorbic acid solution to stabilize the ascorbic acid.

Example 2

[0111] Observation of the Effect of the Addition of a Combination According to the Invention on the Synthesis of Tenascin and of Collagen VII:

[0112] The present example describes the effects of the addition of a combination according to the invention, comprising ascorbic acid and a polymer or copolymer according to the invention, on reconstructed skin by observation with a microscope of a skin section with immunohistochemical labelling of the proteins of tenascin and collagen VII.

[0113] 1. Preparation of the Reconstructed Skin

[0114] The reconstructed skin used is prepared according to the protocol described in Asselineau et al. (Models in Dermato. Published by Loire and Maibach, 1987, Vol III, 1-7). The modifications to this protocol are:

[0115] the use of normal adult human dermal fibroblasts in a proportion of 106 cells per equivalent dermis;

[0116] the inoculation of the keratinocytes is carried out in a proportion of 50 000 cells per ring with a diameter of 1.5 cm. The keratinocytes used originate from the same donor and are at passage 1 during the inoculation of the dermal equivalents;

[0117] the duration of the immersion phase is 7 days;

[0118] the duration of the emergence phase is 7 days.

[0119] 2. Addition of the Combination According to the Invention:

[0120] The final change in medium of the immersion phase is carried out in the presence of the combination of ascorbic acid and of vinylpyrrolidone/vinylimidazole. The culture is subsequently mounted on a grid for the emergence phase (7 days) and, during this phase, all changes in medium (every 2 days) are carried out in the presence of the above combination.

[0121] 3.a. Analysis of Collagen VII

[0122] The reconstructed skins are analysed at the end of the emergence phase. A control sample is systematically prepared and analysed in parallel.

[0123] The samples are taken and frozen in liquid nitrogen. The blocks are produced from Tissue Teck. Collagen of type VII is detected by immunohistochemistry on frozen sections with a thickness of 5 μm. The conventional indirect immunofluorescence technique is carried out with an anti-collagen VII monoclonal antibody (LH7.2, Chemicon International Inc., USA) and a fluorescein-coupled conjugate (FITC-conjugated Rabbit anti mouse immunoglobulins, DAKO, Denmark).

[0124] 3.b. Analysis of Tenascin

[0125] The protocol used is that described in point 3.a. above, except that, in this case, the tenascin is detected with an antitenascin monoclonal antibody (TN2, Chemicon) and a fluorescein-coupled conjugate (FITC-conjugated Rabbit anti mouse immunoglobulins, DAKO, Denmark).

[0126] 4. Observations:

[0127] On observing with a microscope, it is found that the intensity and the thickness of the fluorescence region corresponding to the dermoepidermal junction is much greater in the sample to which the ascorbic acid and vinylpyrrolidone/vinylimidazole copolymer combination has been added. This was observed both for the analysis of collagen VII and for the analysis of tenascin.

Example 3

[0128] O/W Anti-Ageing Cream

[0129] The following composition is prepared in a way conventional to a person skilled in the art.

Water	16 g
Glycerol	3 g
Sorbitan tristearate	0.68 g
PEG-40 stearate	1.5 g
Cetyl alcohol	3 g
Glyceryl stearate	2.25 g
Myristyl myristate	1.5 g
Ethylhexyl palmitate	1.5 g
Hydrogenated polyisobutene	2.5 g
Shorea robusta seed butter	1.5 g
Butyrospermum parkii (shea butter) fruit	0.5 g
Cyclopentasiloxane	7.5 g
Phenoxyethanol	1 g
Water	46.24 g
Ascorbic acid	5 g
Potassium hydroxide (50% solution)	3 g
Vinylpyrrolidone/vinylimidazole copolymer	1 g

[0130] This rich and soft cream makes it possible to combat signs of intrinsic ageing and has good stability for the ascorbic acid.

Example 4

[0131] Anti-Ageing Cream

[0132] The following composition is prepared in a way conventional to a person skilled in the art.

Pentaerythrityl tetraethylhexanoate	6 g
Ammonium polyacryloyldimethyl taurate	0.6 g
Water	14.95 g
Methylparaben	0.2 g
Glycerol	3 g
Phenoxyethanol	0.5 g
PTFE	4 g
Cetearyl alcohol (and) ceteareth-30	1.5 g
Octocrylene	7 g
Butyl methoxydibenzoylmethane	2 g
Ethylhexyl salicylate	5 g
Glycolipids	0.5 g
Propylparaben	0.1 g
Petrolatum	1 g
Polysorbate 60	1 g
Cetyl alcohol	0.5 g
Caprylyl glycol	0.15 g
Glyceryl starch	2 g
Water	41 g
Ascorbic acid	5 g
Potassium hydroxide (50% solution)	3 g
Vinylpyrrolidone/vinylimidazole copolymer	1 g

[0133] This cream which is soft and fresh on application makes it possible to combat wrinkles and fine lines and has a good degree of stabilization for the ascorbic acid.

[0134] The above description of the invention, as illustrated by non-limiting examples, allows one of ordinary skill in this art to make and use, for preventing and/or treating cutaneous signs of intrinsic ageing, a composition comprising, preferably in a physiologically acceptable medium comprising an aqueous phase, at least one oxidation-sensitive hydrophilic active principle for example selected from the group consisting of ascorbic acid and its derivatives and at least one non-crosslinked N-vinylimidazole polymer or copolymer, the active principle and the polymer or copolymer both being present in the aqueous phase. Also provided is the use of a combination comprising at least one oxidation-sensitive hydrophilic active principle selected from the group consisting of ascorbic acid and its derivatives and of at least one non-crosslinked N-vinylimidazole polymer or copolymer in the aqueous phase of a cosmetic composition as an agent for preventing and/or treating cutaneous signs of intrinsic ageing. Also provided is the use of at least one oxidation-sensitive hydrophilic active principle selected from the group consisting of ascorbic acid and its derivatives and of at least one non-crosslinked N-vinylimidazole polymer or copolymer for the preparation of a dermatological composition comprising an aqueous phase which is intended to prevent and/or treat cutaneous signs of intrinsic ageing. Also provided is a cosmetic treatment process intended to prevent and/or treat cutaneous signs of intrinsic ageing, comprising the application, to the skin or mucous membranes, of a composition comprising, preferably in a physiologically acceptable medium comprising an aqueous phase, at least one oxidation-sensitive hydrophilic active principle selected from the group consisting of ascorbic acid and its derivatives and at least one non-crosslinked N-vinylimidazole polymer or copolymer, the active principle and the polymer or copolymer both being in the aqueous phase. Also provided is a method for preventing and/or treating cutaneous signs of intrinsic ageing, comprising applying a composition comprising a physiologically acceptable medium comprising an aqueous phase, at least one oxidation-sensitive hydrophilic active principle selected from the group

consisting of ascorbic acid and its derivatives, and at least one non-crosslinked N-vinylimidazole polymer or copolymer to a cutaneous tissue, the active principle and the polymer or copolymer both being present in the aqueous phase of the composition.

[0135] French patent application 0115375 is incorporated herein by reference, as are all references, texts, documents, patents, applications, standards, etc. mentioned above. Where a numerical range is stated all values therebetween are included as if specifically written out.

[0136] Also incorporated herein by reference are the following U.S. applications, all filed Nov. 27, 2002, where the present application is listed for information only:

[0137] U.S. Serial No. . . . (Atty. Docket 230634US0)

[0138] U.S. Serial No. . . . (Atty. Docket 230608US0)

[0139] U.S. Serial No. . . . (Atty. Docket 230616US0)

[0140] U.S. Serial No. . . . (Atty. Docket 230614US0)

[0141] U.S. Serial No. . . . (Atty. Docket 230615US0)

1. A method for preventing and/or treating cutaneous signs of intrinsic ageing, comprising applying a composition comprising a physiologically acceptable medium comprising an aqueous phase, at least one oxidation-sensitive hydrophilic active principle selected from the group consisting of ascorbic acid and its derivatives, and at least one non-crosslinked N-vinylimidazole polymer or copolymer to a cutaneous tissue, the at least one active principle and the at least one polymer or copolymer both being present in the aqueous phase of the composition.

2. The method according to claim 1, wherein said derivatives of ascorbic acid are selected from the group consisting of esters and salts of ascorbic acid.

3. The method according to claim 1, wherein said composition comprises a derivative of ascorbic acid selected from the group consisting of esters and salts of ascorbic acid.

4. The method according to claim 3, wherein the hydrophilic active principle is selected from the group consisting of 5,6-di-O-dimethylsilylascorbate, dl- α -tocopheryl dl-ascorbyl phosphate potassium salt, magnesium ascorbyl phosphate and sodium ascorbyl phosphate.

5. The method according to claim 1, wherein the oxidation-sensitive hydrophilic active principle is ascorbic acid.

6. The method according to claim 1, wherein the composition comprises a non-crosslinked copolymer that is a combination of the N-vinylimidazole with N-vinylpyrrolidone and/or N-vinylcaprolactam subunits.

7. The method according to claim 1, wherein the composition comprises a non-crosslinked copolymer that is an N-vinylimidazole/N-vinylpyrrolidone copolymer.

8. The method according to claim 1, wherein the composition comprises a non-crosslinked copolymer selected from the group consisting of a vinylpyrrolidone/vinylimidazole (50/50) copolymer having a weight-average molar mass of 1 200 000 and a vinylpyrrolidone/vinylimidazole (50/50) copolymer having a weight-average molar mass of 10 000.

9. The method according to claim 1, wherein a molar ratio of N-vinylimidazole unit equivalent to the oxidation-sensitive hydrophilic active principle is from 0.004 to 16.

10. The method according to claim 9, wherein the molar ratio of the N-vinylimidazole unit equivalent to the oxidation-sensitive hydrophilic active principle is from 0.01 to 1.

11. The method according to claim 1, wherein the polymer or copolymer is present at a concentration of 0.1 to 5% by weight of the aqueous phase.

12. The method according to claim 11, wherein the polymer or copolymer is present at a concentration of 0.1 to 2% by weight of the aqueous phase.

13. The method according to claim 1, wherein the polymer or copolymer has a molar fraction of N-vinylimidazole units of between 0.1 and 1.

14. The method according to claim 13, wherein the polymer or copolymer has a molar fraction of N-vinylimidazole units of between 0.4 and 0.9.

15. The method according to claim 1, wherein the composition further comprises an agent different from said hydrophilic active principle which stimulates dermal macromolecules or which prevents their decomposition and/or an agent different from said hydrophilic active principle which stimulates the proliferation of fibroblasts or keratinocytes and/or the differentiation of keratinocytes.

16. The method according to claim 1, wherein said cutaneous tissue is selected from the group consisting of skin and mucous membranes.

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