

SKIN CARE PRODUCT AND PROCEDURE FOR ITS PRODUCTION

FIELD OF THE INVENTION

[0001] The present invention relates to lipid particles, particularly for use in skin care products.

BACKGROUND OF THE INVENTION

[0002] In recent times, have become widespread skin care products, such as creams, lotions or serums, composed of a fluid substance, usually a gel, which incorporates lipid particles containing one or more molecules of cosmetic active ingredients

[0003] Examples of the aforesaid active ingredients are vitamins, such as for example vitamins A, C, E and their derivatives, coenzyme Q10, minerals, antioxidants, natural extracts and peptides.

[0004] Among the factors known to cause damage to the skin are the so-called "free radicals". These are responsible for lipid peroxidation. Among these, in particular the so-called ROS (Reactive Oxygen Species) containing molecular oxygen with an electron deficiency ("peroxyl"), when in excess, cause damage, the most serious of which is premature aging of the skin.

[0005] In the process of lipid peroxidation the lipids containing unsaturated fatty acids and their esters are directly oxidized by molecular oxygen and the damage is able to propagate through a chain reaction, as the electron-deprived lipids tend to reintegrate the loss by subtracting electrons from the contiguous molecules, up to also involving the proteins of the central nucleus and DNA.

[0006] Following these reactions, some of the possible damages are therefore: lipid peroxidation, peroxidation of amino acids and proteins, enzymatic alterations and damage to protein structures.

[0007] ROS generated within mitochondria can retroact and directly damage mtDNA and other mitochondrial components. ROS can also damage nuclear DNA.

[0008] For all these reasons, the oxidative modification of some proteins can be an important aging factor. Therefore, products containing anti-oxidant active ingredients capable of interacting with ROS and inhibiting their activity are known and widespread. For example, those products are commercialized as:

[0009] - Revitalift® Derm Intensives 10% Pure Vitamin C (L'Oréal Paris),

[0010] - Resveratrol B E Antioxidant Night concentrate (Skinceuticals)

[0011] - DayWear Advanced Multi-Protection Anti-Oxidant Creme SPF 15 (Estee Lauder)

[0012] - Anthelios AOX Daily *Antioxidant* Serum with Sunscreen (La Roche-Posay)

[0013] However, the products available today to reduce ROS in the skin have limitations.

For example, these products, while comprising active ingredients sensitive to ROS, have the drawback that the latter are either in the free state or incorporated in lipid particles that have a stable matrix, i.e. a containment envelope, designed to protect the content, or to vehicle it in a controlled and specific manner but not to have affinity towards ROS.

[0014] This matrix generally consists of predominantly saturated polymers and/or lipids stable to oxidation (Comunian et al. "Protection and controlled release of vitamin C by different micro/nanocarriers", Crit Rev Food Sci Nutr. 2020, Dec 22;1-22).

[0015] The matrices used in the products known to date have the purpose of protecting the active ingredients incorporated, making them more bioavailable, that is able to reach the circulatory system, and increasing skin penetration and gradual release

[0016] For these reasons, however, the activity of the active ingredients is expressed equally on the entire area of skin where the product is applied regardless of the localized concentration of ROS and not preferentially in the areas with a higher concentration of ROS, which are those in which there would be a greater need.

[0017] Furthermore, for the production of similar products, it is necessary to use organic solvents, such as dichloromethane, chloroform, diethyl ether and ether-methanol mixtures which can be toxic, or high temperatures, higher than 60°C and up to 100°C (Ghasemiyeh et al., "Solid lipid nanoparticles and nanostructured lipid carriers as novel drug delivery systems: applications, advantages and disadvantages", Res Pharm Sci.2018 Aug; 13(4):288-303). This results in an economically and energetically expensive process.

BRIEF SUMMARY OF THE INVENTION

[0018] In light of the limitations of the prior art described above, the main aim of the present invention is to provide a product for skin care and a process for its manufacture which are capable of improving the prior art in one or more of the aspects indicated above.

[0019] Within this aim, an object of the invention is to provide lipid particles which have a high sensitivity to ROS and are able to convey the active ingredients incorporated therein in the areas which have ROS and in particular in those with a higher concentration of ROS.

[0020] Another object of the invention is to provide a skin care product with a greater affinity for ROS than similar products known to date. Another object of the invention is to provide a method for manufacturing a skin care product that does not provide for the use of organic solvents and the use of high temperatures.

[0021] Not the least object of the invention is to provide a product for skin care and a process for its manufacture which are highly reliable, relatively easy to implement and at competitive costs.

[0022] This task, as well as these and other purposes which will be apparent later, are achieved by lipid particles wherein each of said particles comprises:

[0023] - (a) a matrix, comprising:

[0024] (i) from greater than or equal to 20% to less than or equal to 60% by weight on the total weight of the lipid particle, of a lipid component characterized by a melting temperature from greater than or equal to 40°C to less than or equal to 55°C;

[0025] (ii) from greater than or equal to 20% to less than or equal to 30% by weight on the total weight of the lipid particle of one or more unsaturated fatty acids;

[0026] (iii) from greater than or equal to 10% to less than or equal to 12% by weight on the total weight of the lipid particle of one or more excipients selected from surfactants, suspending agents, humectants and their mixtures;

[0027] and (b) at least one antioxidant agent, incorporated in said matrix.

[0028] The aims and objects of the present invention are also achieved by a process for the preparation of lipid particles according to the invention, comprising the steps of:

[0029] (i) melting the lipid component;

[0030] (ii) dispersing the one or more unsaturated fatty acids in the fused lipid component of step (i);

[0031] (iii) dispersing in water previously heated to a temperature from greater than or equal to 40°C to less than or equal to 50°C:

[0032] - the at least one antioxidant agent; and

[0033] - the one or more excipients;

[0034] (iv) adding said dispersion obtained in step (ii) to said aqueous dispersion obtained in step (iii), under stirring, obtaining an emulsion;

[0035] (v) cooling the emulsion obtained in step (iv) to a temperature from greater than or equal to 5°C to less than or equal to 15°C, obtaining an emulsion consisting of lipid particles in an aqueous phase.

[0036] Furthermore, the tasks and purposes of the invention are also achieved by lipid particles for use in the topical treatment of a condition associated with an accumulation of ROS ("Reactive Oxygen Species") in the skin of a patient, wherein each of said lipid particles comprises:

[0037] (a) a matrix comprising:

[0038] (i) a lipid component;

[0039] (ii) one or more unsaturated fatty acids;

[0040] (iii) one or more excipients selected from surfactants, suspending agents, humectants and their mixtures;

[0041] and

[0042] (b) at least one antioxidant agent, incorporated in said matrix.

[0043] The aims and objects of the present invention are also achieved by a skin care product comprising the lipid particles according to the invention.

[0044] Finally, the aims and objects of the invention are also achieved by lipid particles according to the invention or a skin care product according to the invention for use in the topical treatment of a condition associated with an accumulation of ROS in a patient's skin.

[0045] Further characteristics and advantages of the invention will become clearer from the following detailed description.

DETAILED DESCRIPTION

[0046] In a first aspect, the present invention relates to lipid particles wherein each of said particles comprises a matrix and at least one antioxidant agent incorporated therein.

[0047] The matrix of the lipid particles of the invention comprises from greater than or equal to 20% to less than or equal to 60% by weight on the total weight of the lipid particle, of a lipid component having a melting temperature from greater than or equal to 40°C to less than or equal to 55°C.

[0048] Advantageously, the aforementioned melting temperature is closer to the temperature of the skin (37°C) than the melting temperatures of other waxes used to create lipid particles such as microcrystalline wax, carnauba wax, bees wax, that have a melting temperature above 65°C.

[0049] In a preferred embodiment, the lipid component is a mixture of at least two of mimosa wax (acacia decurrens), jojoba seed wax, sunflower seed wax, polyglycerol, pentaerythrityl distearate, and transesterification products of polyglycerol and at least one wax chosen from jojoba wax, mimosa wax and sunflower seed wax.

[0050] Furthermore, the matrix of the lipid particles according to the invention comprises (ii) from greater than or equal to 20% to less than or equal to 30% by weight on the total weight of the lipid particle of one or more unsaturated or preferably polyunsaturated fatty acids which by having a high affinity towards ROS, provide the lipid particles of the invention with the property of interacting with ROS, releasing the active ingredients in a targeted manner. The lipid particles of the invention have a matrix therefore characterized by a high affinity towards ROS.

[0051] In the present description, the term "affinity" means the tendency that the active principles or lipid particles that comprise them have to interact with ROS.

[0052] As described above, ROS affinity is measured by the iodine index.

[0053] As described above, the lipid particles commonly used today have an oxidation stable matrix.

[0054] In the present description, the expression "stable matrix" means a matrix stable to oxidation and, in the case of a lipid matrix, this means an iodine index less than 60g Iodine/100g, where the iodine index is measured according to ASTM D1959-97 standard.

[0055] In a preferred embodiment, the matrix of the lipid particles according to the invention has an iodine index higher or equal to 60g Iodine/100g where the iodine index is measured according to the ASTM D1959-97 standard.

[0056] The matrix of the particles of the invention comprises one or more unsaturated fatty acids, preferably selected from the group consisting of C16-C24 unsaturated fatty acids and their mixtures. In a preferred embodiment, said one or more unsaturated fatty acids are selected from the group consisting of linoleic acid, linolenic acid, alpha linolenic acid, oleic acid and their mixtures.

[0057] Preferably the one or more unsaturated fatty acids of the matrix comprise at least 60% by weight of polyunsaturated fatty acids on the total weight of the unsaturated fatty acids.

[0058] The lipid particles of the invention comprise at least one antioxidant agent, incorporated in the matrix.

[0059] Preferably the at least one antioxidant agent is selected from the group consisting of BHT (butylhydroxytoluene), vitamin E, vitamin C, BHA (butylhydroxyanisole), polyphenols, carotenoids, superoxide dismutase and bisulfites.

[0060] In the context of the present description, the term "vitamin C" refers to ascorbic acid and its derivatives such as, for example, sodium ascorbyl phosphate, ascorbyl tetraisoalmitate, 3-O-cetyl ascorbic acid and ascorbyl glucoside.

[0061] The matrix of the lipid particle, rich in unsaturated and polyunsaturated fatty acids which provide a high affinity towards ROS, therefore allows to selectively convey the antioxidant agents incorporated in it, and to act as "scavengers" in skin areas rich in ROS allowing therefore to neutralize them.

[0062] Preferably in the lipid particles of the invention the at least one antioxidant is in an amount comprised from greater than or equal to 5% to less than or equal to 20% by weight on the total weight of the lipid particle.

[0063] The matrix of the lipid particles according to the invention further comprises (iii) from greater than or equal to 10% to less than or equal to 12% by weight on the total weight of the lipid particle of one or more excipients selected from surfactants, suspending agents, humectants and their mixtures.

[0064] Preferably, the at least one excipient is selected from the group consisting of polysorbates, polyacrylates, xanthan gum, alkyl glucosides and glycols.

[0065] Furthermore, the lipid particles of the invention can further comprise one or more active ingredients incorporated in said matrix, wherein the one or more active ingredients are selected from the group consisting of vitamins, peptides, minerals, growth factors and natural extracts.

[0066] The aforementioned active ingredients have the function of restoring the physiological balance, repairing and stimulating the autogenous repair mechanisms of the skin damaged by excessive concentrations of ROS.

[0067] The term “active ingredient” in this description refers to a substance which possesses a biological activity or which influences the appearance and conditions of the skin.

[0068] With the expression “biological activity”, in the present description, it is meant that this substance has an effect on a biological tissue, in this case the skin, or a cosmetic effect on it.

[0069] In a second aspect, the present invention relates to a process for the preparation of lipid particles according to the invention, comprising the steps of:

[0070] (i) melting the lipid component;

[0071] (ii) dispersing the one or more unsaturated fatty acids in the fused lipid component of step (i);

[0072] (iii) dispersing in water previously heated to a temperature from greater than or equal to 40°C to less than or equal to 50°C:

[0073] - the at least one antioxidant agent; and

[0074] - the one or more excipients;

[0075] (iv) adding said dispersion obtained in step (ii) to said aqueous dispersion obtained in step (iii), under stirring, obtaining an emulsion;

[0076] (v) cooling the emulsion obtained in step (iv) to a temperature from greater than or equal to 5°C to less than or equal to 15°C, obtaining an emulsion consisting of lipid particles in an aqueous phase.

[0077] In step (iv) the stirring is preferably carried out at a constant speed between 1000 and 8000 revolutions per minute.

[0078] Preferably, before step (v) the emulsion obtained in step (iv) is sieved through a net with holes ranging in size from greater than or equal to 0.1 to less than or equal to 50µm, obtaining an emulsion consisting of lipid particles in an aqueous phase with a size ranging from greater than or equal to 0.1 to less than or equal to 50µm. Said emulsion, after cooling in step (v), can then be dried under vacuum at a temperature below 40°C and/or stabilized by adding preservatives such as, for example, sodium benzoate, potassium sorbate, isothiazolinones, phenoxyethanol, formaldehyde eliminators, chelating agents.

[0079] In a preferred embodiment of the process according to the invention, the lipid component is a mixture of at least two of mimosa wax (*acacia decurrens*), jojoba seed wax, sunflower seed wax, polyglycerol, pentaerythrityl distearate, transesterification products of polyglycerol 3 and at least one wax chosen from jojoba wax, mimosa wax and sunflower seed wax;

[0080] The choice of the above described mixture of waxes advantageously allows the particles to be prepared with a process which does not require high temperatures or organic solvents.

[0081] In a preferred embodiment, the process according to the invention does not include the use of organic solvents.

[0082] The lipid particles of the invention obtained as described above can then be incorporated into a skin care product selected from the group consisting of a serum, a cream and a lotion, mixing them with said skin care product at a temperature less than or equal to 40°C and a speed between 100 and 200 revolutions per minute until complete homogenization.

[0083] The present invention therefore also relates to a skin care product comprising the lipid particles according to the invention. Said product, preferably chosen from a serum, a cream and a lotion, optionally packaged in airtight containers, is protected from the formation of ROS inside it.

[0084] The present invention also relates to the lipid particles described above and to the skin care product described above for use in the topical treatment of a condition associated with an accumulation of ROS in the skin of a patient.

[0085] Skin conditions associated with ROS accumulation include premature aging, loss of elasticity, loss of hydration, hyperpigmentation, dyschromia, acne, and imbalance of physiological balance.

[0086] The present invention also refers to lipid particles for use in the topical treatment of a condition associated with an accumulation of ROS in the skin of a patient, wherein each lipid particle comprises:

[0087] (a) a matrix comprising:

[0088] (i) a lipid component;

[0089] (ii) one or more unsaturated fatty acids;

[0090] (iii) one or more excipients selected from surfactants, suspending agents, humectants and their mixtures;

[0091] and

[0092] (b) at least antioxidant agent, incorporated in said matrix.

[0093] The present invention relates of course also to a method for treating a condition associated with an accumulation of ROS in the skin of a patient, by applying to a patient the lipid particles or the skin care product described above.

[0094] The invention will now be described with reference to the following non-limiting example.

[0095] Example 1: Preparation of lipid particles of the invention.

[0096] To prepare 1kg of a composition comprising the lipid particles of the invention, to be used as an intermediate in the preparation of cosmetic products, the procedure was as follows:

[0097] (i) 90g of a blend of jojoba wax, mimosa wax and sunflower seed wax (ACTICIRE® MB, ACTICIRE-GATTE FOSSE) and 30g of a blend of natural polyunsaturated fatty acids obtained from safflower oil (Vitamin F forte, CLR Berlin) were melted in a beaker by heating at a temperature of 55°C under magnetic stirring at 200 rpm for 10 minutes until the phase was completely melted;

[0098] (ii) 30g of a mixture of natural polyunsaturated fatty acids obtained from safflower oil (Vitamin F forte, CLR Berlin) were added to the melted lipid mixture obtained in step (i), under magnetic stirring at 200 rpm while maintaining the temperature at 55°C, until a homogeneous “fat” melted mixture is obtained;

[0099] (iii) an aqueous dispersion was prepared by adding to 758ml of water heated to 45°C subsequently under stirring (500 rpm for 10 min):

[00100] - 20g of decyl glucoside,

[00101] - 100g of sodium ascorbyl phosphate,

[00102] - 2g of hyaluronic acid;

[00103] (iv) the aqueous dispersion prepared in point (iii) was added to the fat mixture prepared in point (ii) by maintaining the temperature at 48°C under stirring at 3500 rpm for 10 minutes, obtaining an emulsion of lipid particles in a aqueous phase;

[00104] (iv-a) the emulsion obtained in step (iv) was sieved through a net with pores with a diameter of 25µm, obtaining an emulsion of lipid particles with a diameter of up to 25µm in an aqueous phase;

[00105] (v) the emulsion obtained in step (iv-a) was cooled to 10°C by means of a water bath to accelerate the solidification of the lipid part;

[00106] In practice it has been found that the invention achieves the intended aim and objects by producing lipid particles and skin care products characterized by a high affinity for ROS and capable of conveying the active ingredients incorporated therein into the matrix of the lipid particles in the areas with ROS and in particular in those with a higher concentration of ROS.

[00107] The skin care products which incorporate the lipid particles according to the invention advantageously have a greater affinity towards ROS than analogous products on the market today.

[00108] Furthermore, the invention has perfected a process for manufacturing a skin care product which does not involve the use of organic solvents and the use of high temperatures.

[00109] The invention thus conceived is susceptible of numerous modifications and variations, all of which are within the scope of the inventive concept; moreover, all the details can be replaced by other technically equivalent elements.

[00110] In practice, the materials employed, so long as they are compatible with the specific use, as well as the contingent shapes and dimensions, may be any according to requirements and to the state of the art.

CLAIMS

We claim:

1. Lipid particles wherein each particle comprises:

- (a) a matrix, comprising:

(i) from greater than or equal to 20% to less than or equal to 60% by weight on the total weight of the lipid particle, of a lipid component having a melting temperature from greater than or equal to 40°C to less than or equal to 55°C;

(ii) from greater than or equal to 20% to less than or equal to 30% by weight on the total weight of the lipid particle of one or more unsaturated fatty acids;

(iii) from greater than or equal to 10% to less than or equal to 12% on the total weight of the lipid particle of one or more excipients selected from surfactants, suspending agents, humectants and their mixtures;

and (b) at least one antioxidant agent, incorporated in said matrix.

2. Lipid particles according to claim 1 where said lipid component is a mixture of at least two of mimosa wax (*acacia decurrens*), jojoba seed wax, sunflower seed wax, polyglycerol, pentaerythrityl distearate, and transesterification products of polyglycerol and at least one wax chosen from jojoba wax, mimosa wax and sunflower seed wax.

3. Lipid particles according to claim 1 or 2, wherein said matrix has an iodine index greater than or equal to 60g Iodine/100g where the iodine index is measured according to the ASTM D1959-97 standard.

4. Lipid particles according to one or more of the preceding claims, wherein the one or more unsaturated fatty acids comprise at least 60% of polyunsaturated fatty acids by weight on the total weight of unsaturated fatty acids.

5. Lipid particles according to one or more of the preceding claims, wherein the at least one antioxidant agent is in an amount from greater than or equal to 5% to less than or equal to 20% by weight on the total weight of the lipid particle.

6. Lipid particles according to one or more of the preceding claims, wherein said one or more unsaturated fatty acids are selected from the group consisting of C16-C24 fatty acids and their mixtures.

7. Lipid particles according to one or more of the preceding claims, wherein the at least one excipient is selected from the group consisting of polysorbates, polyacrylates, xanthan gum, alkyl glucosides and glycols.

8. Lipid particles according to one or more of the preceding claims, wherein the at least one antioxidant agent is selected from the group consisting of BHT (butylhydroxytoluene), vitamin E, vitamin C, BHA (butylhydroxyanisole), polyphenols, carotenoids, superoxide dismutase and bisulfites.

9. Lipid particles according to one or more of the preceding claims further comprising one or more active ingredients incorporated in said matrix, wherein the one or more active

ingredients are selected from the group consisting of vitamins, peptides, minerals, growth factors and natural extracts.

10. Process for the preparation of lipid particles according to the invention, comprising the steps of:

(i) melting the lipid component;

(ii) dispersing the one or more unsaturated fatty acids in the fused lipid component of step (i);

(iii) dispersing in water previously heated to a temperature from greater than or equal to 40°C to less than or equal to 50°C:

- the at least one antioxidant agent; and

- the one or more excipients;

(iv) adding said dispersion obtained in step (ii) to said aqueous dispersion obtained in step (iii), under stirring, obtaining an emulsion;

(v) cooling the emulsion obtained in step (iv) to a temperature from greater than or equal to 5°C to less than or equal to 15°C, obtaining an emulsion consisting of lipid particles in an aqueous phase.

11. Process according to claim 10 wherein said process does not comprise the use of organic solvents.

12. Lipid particles for use in the topical treatment of a condition associated with an accumulation of ROS ("Reactive Oxygen Species") in the skin of a patient, wherein each lipid particle comprises:

(a) a matrix comprising:

(i) a lipid component;

(ii) one or more unsaturated fatty acids;

(iii) one or more excipients selected from surfactants, suspending agents, humectants and their mixtures;

and

(b) at least one antioxidant agent, incorporated in said matrix.

13. Skin care product comprising the lipid particles according to one or more of claims 1-9.

14 Lipid particles according to one or more of claims 1-9 or skin care product according to claim 13 for use in the topical treatment of a condition associated with an accumulation of ROS in the skin of a patient.