the skin, such as skin atrophy, skin dyspigmentation (patches/spots), photodermatitis (erythema: inflamed and reddened skin), telangiectasia, (couperose) and UV prevention to avoid skin erythema and actinic keratosis [figure 2].

Thus applicants provide a new composition comprising vitamin D3 or a derivative or precursor thereof, preferably a precursor such as 7-DHC or a derivative thereof and HA or derivatives, optionally in combination with additional excipients, encapsulated in a lipid based colloidal carrier system (preferably lipid based vesicles such as liposomes, niosomes, tranferosomes) to allow the penetration and localized delivery of stabilized vitamin D3 or a derivative or precursor thereof, preferably a precursor such as 7-DHC or a derivative thereof into the upper layers of the skin.

The two active substances combined topically are able to act in a synergistic manner directly in the upper layers of the skin on the dominant disorders of inflamed skin, expecially in photodamage, in particular on the indication according ICD-10 of sun and exspecially UV radiation exposed and damaged skin. Thus the new composition of the invention is able to overcome drawbacks of prior art. The additional seven excipients will act synergistic with the two active substances and allow an optimal efficacy to prevent and/or treat the described skin disorders. The described composition (and formulations thereof) will provide a new approach to prevent and/or treat most disorders of inflamed skin, sun and exspecially UV radiation damaged skin [figures 2, 3].

Summary

The disclosure is directed towards a new composition (also referred to as composition of the disclosure) comprising a synergistic combination of at least one vitamin D3 or a derivative or precursor thereof, preferably a precursor such as 7-DHC or a derivative thereof and at least one HA or derivative thereof, encapsulated in a lipid based colloidal carrier system (to allow for optimal skin penetration and stabilization of the vitamin D3 or a precursor or derivative thereof) and suitable formulations thereof. By encapsulation in the oil (or lipid) phase the vitamin D3 or a precursor or derivative thereof (and in particular 7-DHC or a derivative thereof) is stabilized and undesired reactions (such as oxidation or other degradation reactions) are eliminated. The lipid based colloidal carrier system allows vitamin D3 (and inactive vitamin D3 precursors such as 7-DHC or a derivative thereof) to penetrate into the upper layers of the skin, where exerts its activity (after being converted into the active vitamin D3 upon UVA and UVB exposure).

In a preferred example the vitamin D3 is a vitamin D3 precursor such as 7-DHC or a derivative thereof, and the composition of the disclosure comprises a vitamin D precursor such as 7-DHC or a derivative thereof, in combination with HA or a derivative thereof encapsulated in a lipid based colloidal carrier system. The vitamin D (and in particular the vitamin D3 precursor such as 7-DHC or a derivative thereof) is preferably present in the colloidal carrier system at a final concentration of 0.01 to 0.5 wt%.

Thus, in one aspect, the present disclosure provides a composition comprising at least one vitamin D3 or precursor or derivative thereof and at least one hyaluronic acid or derivative thereof encapsulated in a lipid based colloidal carrier system, wherein the at least one vitamin D3 or precursor or derivative thereof is selected from vitamin D3, 7-DHC, 25-hydroxyvitamin D3, 1a,25-dihydroxyvitamin D3, and 1a-hydroxyvitamin D3 and wherein the at least one hyaluronic acid or derivative thereof is a mixture of low molecular weight hyaluronic acid of 4 kDa to 40 kDa and higher molecular weight hyaluronic acid up to 200'000 kDa.

In other examples the composition further comprises one or more, preferably 1, 2, 3, 4, 5, 6, 7 further components selected from a vitamin A (preferably retinyl palmitate), at least one vitamin B, a vitamin C (preferably L-ascorbic acid) and a vitamin E (preferably tocopheryl acetate). Preferably, the composition further comprises one or more, most preferably all, of (i) retinyl palmitate (vitamin A), (ii) riboflavin (vitamin B2), (iii) niacinamide (vitamin B3), (iv) dexpanthenol (Provitamin B5), (v) folic acid (vitamin B9), (vi) L-ascorbic acid (vitamin C) and (vii) tocopheryl acetate (vitamin E).

In another specific example, the lipid based colloidal carrier system is a liposomal carrier system (preferably a lipid based vesicle such as liposome, niosome, tranferosome) composed of at least one phospholipid and at least one fatty acid. Preferably the lipid based colloidal carrier system comprises one or more of e.g. lecithin, linolenic acid, linoleic acid, phosphatidylcholine and caprylic/capric triglyceride.

In a preferred example, the lipid based colloidal carrier (e.g. a lipid based vesicle such as liposome, niosome, tranferosome) comprises the synergistic combination of 7-DHC and HA in combination with the two lipophilic agents retinyl palmitate (Vitamin A), tocopheryl acetate (Vitamin E), and the five hydrophilic agents riboflavin (Vitamin B2), niacinamide (Vitamin B3), dexpanthenol (Provitamin B5), folic acid (Vitamin B9), L-ascorbic acid (Vitamin C).

The lipophilic agents are encapsulated within the bilayer or multilamellar system, whereas the hydrophilic agents are encapsulated in the aqueous phase. Thus, in one example the composition of the disclosure is obtained by (i) encapsulating the vitamin D_3 (and in particular vitamin D_3 precursor such as 7-DHC or a derivative thereof) in the oil (or lipid) phase of the lipid based colloidal carrier system at room temperatures, and (ii) separately preparing HA in the aqueous phase. The comnpositions are obtained by emulsification of the water phase with the oil (or lipid) phase (by mixing or spontaneopus integration at room

temperature). Preferably, the particles will have a diameter of 10–500 nm, more preferably 10-300 nm, most preferably 20–150 nm.

The composition of the disclosure is in form of various formulations suitable for topical or transdermal and mucosa administration. These topical formulations contain the pharmaceutical composition of the disclosure, as well as further auxiliary agents, such as buffering agents, preserving agents and the like. Typical formulations include hydrogels, liogels, hydrolotions, lipolotions, crèmes, ointments, and the like.

In another aspect, the present disclosure provides a topical formulation comprising a composition as described herein in solid, liquid or semisolid form.

In another aspect, the present disclosure provides a topical formulation comprising a composition as described herein in form of emulsions, microemulsions, aqueous dispersions, oils, milks, balsams, foams, aqueous or oily lotions, aqueous or oily gels, creams, solutions, hydroalcoholic solutions, hydroglycolic solutions, hydrogels, serums, ointments, mousses, pastes, sprays or aerosols, or transdermal patches.

The disclosure is directed towards the use of the composition of the disclosure (and topical formulations thereof) in the prevention and/or treatment of skin photo damage symptoms, in particular in the prevention and/or treatment of skin atrophy, skin dyspigmentation (patches/spots), photodermatitis (erythema: inflamated and reddened skin), telangiectasia, (couperose), prevention of photodermatitis (erythema: inflammation of the skin), actinic keratosis and skin UVA and UVB protection.

In another aspect, the present disclosure provides an agent for use in preventing or treating skin disorders comprising a composition as described herein.

Brief Description of Figures

Figure 1: Adequate concentrations of the inactive precursor 7-DHC is transported in form of a lipid-based colloid according to the invention in the upper layers of the skin, where it is converted to active vitamin D3 upon UVA and UVB exposure.

Figure 2: 7-DHC in the oil (or lipid) phase and hyaluronic acid (HA) in the water phase are integrated into the colloidal carrier system, which allows the penetration into the upper layers of the skin. With the activation and synthesis of vitamin D3 from 7-DHC the pathway of skin damages by sunlight UVA/UVB can be blocked. Inactive 7-DHC is protected from oxidative processes with the encapsulation into the carrier system and further being only activated at the target into the upper layers of the skin having a potent function eliminating cytotoxic ROS as peroxynitrates, resulting from the oxidative processes of nitrates. This scavenger function of in excess produced NO's allows the protection of skin damages from UVA/UVB.

Figure 3: 7-DHC pathway of potent anti inflammation activity in the upper layers of the skin after being activated to vitamin D3

Detailed Description

Claims:

1. A composition comprising at least one vitamin D_3 or precursor or derivative thereof and at least one hyaluronic acid or derivative thereof encapsulated in a lipid based colloidal carrier system, wherein the at least one vitamin D_3 or precursor or derivative thereof is selected from vitamin D_3, 7-DHC, 25-hydroxyvitamin D_3, 1α,25-dihydroxyvitamin D_3, and 1α-hydroxyvitamin D_3 and wherein the at least one hyaluronic acid or derivative thereof is a mixture of low molecular weight hyaluronic acid of 4 kDa to 40 kDa and higher molecular weight hyaluronic acid up to 200'000 kDa.

2. A composition according to claim 1 wherein the at least one vitamin D_3 or precursor or derivative thereof is 7-DHC.

3. A composition according to claim 1 wherein the lipid based colloidal carrier system is selected from liposomes, niosomes, transferosomes, micelles, nanoparticles, and microemulsions.

4. A composition according to any preceding claim further comprising one or more further components selected from a vitamin A, at least one vitamin B, a vitamin C and a vitamin E.

5. A composition according to claim 4 wherein the at least one vitamin B is riboflavin (vitamin B_2), niacinamide (vitamin B_3), dexpanthenol (Provitamin B_5), and/or folic acid (vitamin B_9).

6. A composition according to claim 1 further comprising i) retinyl palmitate (vitamin A), (ii) riboflavin (vitamin B_2), (iii) niacinamide (vitamin B_3), (iv) dexpanthenol (Provitamin B_5), (v) folic acid (vitamin B_9), (vi) L-ascorbic acid (vitamin C) and (vii) tocopheryl acetate (vitamin E).

7. A composition according to any preceding claim further comprising at least one UV-filter.

8. A composition according to any preceding claim further comprising at least one adjuvant selected from surfactants, emulsifying agents, emollients, thickening agents, conditioning conservants, buffering agents, humectants, perfuming agents.

9. A composition according to claim 8 wherein the surfactant is a polycarbonate, polyvinylpyrrolidon (PVP), polyvidon, ovidonmembranes, povidone, copovidone, hypromellose or Eudragit EPO.

10. A composition according to claim 8 wherein the surfactant is a polysorbate 10 – 150.

11. A composition according to any preceding claim wherein the lipid based colloidal carrier system is composed of one or more components selected from phospholipids, lecithin, sphingomyelin, linolenic acid, linoleic acid, phosphatidylcholine and caprylic/capric triglyceride.

12. A topical formulation comprising a composition according to claims 1 to 11 in solid, liquid or semisolid form.

13. A topical formulation comprising a composition according to claims 1 to 11 in form of emulsions, microemulsions, aqueous dispersions, oils, milks, balsams, foams, aqueous or oily lotions, aqueous or oily gels, creams, solutions, hydroalcoholic solutions, hydroglycolic solutions, hydrogels, serums, ointments, mousses, pastes, sprays or aerosols, or transdermal patches.

14. An agent for use in preventing or treating skin disorders comprising a composition according to claims 1 to 11.

15. An agent for use in preventing or treating according to claim 14, wherein the skin disorders are selected from inflamed skin, eczema, rosacea, atopic dermatitis, psoriasis, photodamage, skin atrophy, skin dyspigmentation, photodermatitis, telangiectasia (couperose), actinic keratosis.

16. An agent for use in preventing or treating according to claim 14 or 15, which is a topical formulation according to claim 12 or 13.