include pain, erythema, swelling, edema, burning, itching, exfoliation, hyperpigmentation and prolonged irritation and hypersensitivity after treatment. Such side-effects are particularly undesirable when the treatment site is the face, scalp or neck. This is frequently the case when the PDT is for the treatment of lesions (e.g. actinic keratosis, acne, basal cell carcinoma, warts, psoriasis, rosacea, wound healing, squamous cell carcinoma *in situ* or other hyperproliferating or infectious disorders) and when PDT is performed using short-term illumination with high-power light sources. In particular the often substantive pain experienced by the patients in these circumstances results in poor acceptance of this treatment, in particular if PDT has to be applied more than once or on extended skin regions.

An alternative treatment is daylight PDT, which uses sun light with increased exposure time to activate the photosensitizer instead of the high-power light sources used in conventional PDT. The side effects of daylight PDT, in particular the pain, are significantly reduced (Dirschka et al., J Eur Acad Dermatol Venereol. 2018 Jul 19). While the efficacy of daylight PDT seems comparable to conventional PDT, the recurrene rate is significantly higher in daylight PDT.

The present invention teaches the use of photosensitizers in an improved PDT comprising two different light exposures. The present invention therefore provides inter alia the advantages of reduced side effects, in particular reduced pain, and a low recurrence rate.

Summary

In one aspect, the present disclosure provides a use of a composition comprising a photosensitizer in the manufacture of a medicament for preventing or treating a dermatological disease in a patient, , wherein the photosensitizer is selected from 5-aminolevulinic acid (ALA), ALA salts, ALA-esters and their derivatives, and wherein the composition is to be used in the following order of steps: (a) said composition is to be topically applied or subcutaneously injected to an area of the skin of said patient, (b) exposure of at least said area of the skin to sun light, wherein step (b) is carried out outside or inside adjacent to a window, light having a wavelength spectrum of 100 nm to 1000 nm, light having a wavelength spectrum of 380 nm to 780 nm, and/or light having a wavelength spectrum of 570 nm to 650 nm or 570 nm to 630 nm for a duration of 30 min to 5 hours, preferably 1 to 3 hours, more preferably 1 to 2 hours, wherein the light used in step (b) results in a radiant exposure of 10-75 J/cm^2 and (c) exposure of at least said area of the skin to light of a narrower wavelength spectrum compared

Claims

1. Use of a composition comprising a photosensitizer in the manufacture of a medicament for preventing or treating a dermatological disease in a patient, wherein the photosensitizer is selected from 5-aminolevulinic acid (ALA), ALA salts, ALA-esters and their derivatives, and wherein the composition is to be used in the following order of steps:
   (a) said composition is to be topically applied or subcutaneously injected to an area of the skin of said patient,
   (b) exposure of at least said area of the skin to
      - sun light, wherein step (b) is carried out outside or inside adjacent to a window,
      - light having a wavelength spectrum of 100 nm to 1000 nm,
      - light having a wavelength spectrum of 380 nm to 780 nm, and/or
      - light having a wavelength spectrum of 570 nm to 650 nm or 570 nm to 630 nm

      for a duration of 30 min to 5 hours, preferably 1 to 3 hours, more preferably 1 to 2 hours, wherein the light used in step (b) results in a radiant exposure of 10-75 J/cm^2 and
   (c) exposure of at least said area of the skin to light of a narrower wavelength spectrum compared to step (b), preferably comprising only one maximum in the absorbance spectrum of said photosensitizer.

2. The use according to claim 1, wherein the light used in step (c) is red light or violet light.

3. The use according to any one of the preceding claims, wherein the area of the skin comprises skin affected by the disease or skin prone to be affected by the disease.

4. The use according to any one of the preceding claims, wherein there is a residence time interval subsequent to step (a) and prior to step (b) of 1 to 90 min, in particular of 15 to 30 min, preferably in the absence of light exposure.

5. The use according to any one of the preceding claims, wherein the light used in step (b) has an irradiance that is similar to that of average sunlight.

6. The use according to any one of the preceding claims, wherein:

- the light of step (c) has a wavelength in the range of 570 nm to 750 nm, preferably of 570 nm to 670 nm, more preferably of about 635 nm; or
- the light of step (c) has a wavelength in the range of 360 nm to 495 nm, preferably 360 nm to 460 nm, more preferably of about 410 nm.

7. The use according to any one of the claims 2 to 6, wherein:
   - the red light of step (c) results in a radiant exposure of 10-75 J/cm^2, preferably of 25-45 J/cm^2;
   - the violet light of step (c) results in a radiant exposure of 1-30 J/cm^2, preferably 5 to 15 J/cm^2.

8. The use according to any one of the preceding claims, wherein the light used in step (b) has a lower irradiance than the light used in step (c), preferably the irradiance is 2- to 15-times lower than step (c).

9. The use according to any one of the preceding claims, wherein the exposure of step (c) has a duration of at least 5 minutes, preferably of 5-60 minutes, more preferably 10-30 minutes.

10. The use according to any one of the preceding claims, wherein the ALA-ester is selected from methyl-5-amino-4-oxopentanoat and hexyl-5-amino-4-oxopentanoat.

11. The use according to any one of the preceding claims, wherein the composition is formulated as a nanoemulsion additionally comprising:
    (a) at least one aqueous component, and
    (b) a carrier, which comprises:
        (i) at least one lipophilic component,
        (ii) at least one surfactant and
        (iii) at least one alcohol.

12. The use according to claim 11, wherein
    - the carrier is present in the aqueous component and/or

- the surfactant is present in an amount of from 1 % by weight to 30% by weight and the alcohol is present in an amount of from 0.1 % by weight to 10% by weight, based on the total weight of the nanoemulsion.

13. The use according to any one of claims 11 or 12, wherein the aqueous component is present in an amount of from 50% by weight to 98% by weight, based on the total weight of the nanoemulsion.

14. The use according to any one of claims 11 to 13, wherein:
    - the at least one alcohol is isopropylalcohol and/or 1-propylalcohol and/or
    - the at least one lipophilic component are triglycerides and/or a mixture thereof and/or
    - the at least one surfactant is lecithin and/or a polyoxyethylene-type surfactant and/or
    - the mean diameter of the emulsified particles ranges from 10 to 100 nm.

15. The use according to any one of the preceding claims, wherein the dermatological disease is a hyperproliferative disease, preferably keratosis, more preferably actinic keratosis, basal cell carcinoma, or squamous cell carcinoma in situ, or an inflammatory or infectious dermatological condition, preferably warts, acne, or rosacea.

16. Kit of parts comprising a light source capable of emitting light as defined in step (b) and (c) of claim 1 and an instruction manual for carrying out steps (b) and (c) of the use of claim 1.

17. A light source capable of emitting light as defined in step (b) and (c) of claim 1 and a controller, wherein the controller is programmed for carrying out steps (b) and (c) of the use of claim 1.