



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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| <b>(54) Title:</b> COMPOSITIONS AND USES THEREOF<br><br><b>(57) Abstract</b><br><br><p>A sunscreen composition comprising a stearidonic acid, or a physiologically derivative thereof, in combination with a UV blocking and/or UV absorbing material. Also stearidonic acid may be used to treat inflammation caused by exposure to UV radiation, by exposure to sunlight or by burns.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |

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## COMPOSITIONS AND USES THEREOF

This invention relates to certain new compositions, some of which are pharmaceutical compositions. More particularly, the invention relates to compositions  
5 containing stearidonic acid or derivatives thereof. The invention also relates to the use of such compositions.

Ultraviolet (UV) light in the wavelength range of 290 nm to 340 nm is covered by the ranges UVB (290 nm to 320 nm) and UVA2 (320 nm to 340 nm); UV light in this range is erythemogenic. Exposure to small amount of UVB can be  
10 beneficial, since it is required for synthesis of vitamin D in the skin. However, larger amounts of UV radiation cause sunburn, which is characterised by erythema, pain, swelling and blistering; in extreme cases there is epidermal necrosis.

Sunburn is a classical cutaneous inflammation whose pathogenesis is not completely understood. The release of inflammatory mediators including eicosanoids  
15 and cytokines seems to be important. UVB exposure can also compromise the immune system. Chronic UV exposure results in accelerated skin aging called photoaging; it can also lead to the development of skin cancer. The major target in UV induced carcinogenesis is probably DNA. However, the suppressed immune system could play an important role in the pathogenesis of these neoplasms. In  
20 addition to necrosis induced by UV exposure, there is evidence that even acute exposure can result in apoptosis (programmed cell death) of affected keratinocytes.

Cutaneous inflammation caused by UVB is mediated by various cytokines such as tumour necrosis factor-alpha (TNF $\alpha$ ) and interleukin 1 $\alpha$  (IL1 $\alpha$ ). In addition, UVB induces the release of arachidonic acid from cell membrane  
25 phospholipids, which is oxidised via the lipoxygenase and cyclooxygenase pathways to inflammatory metabolites; examples of these include leukotriene B<sub>4</sub> (LTB<sub>4</sub>) and prostaglandin E<sub>2</sub> (PGE<sub>2</sub>). Since human keratinocytes lack the components to produce LTB<sub>4</sub>, PGE<sub>2</sub> is probably the more important inflammatory metabolite in epidermis.

We have now found that, unexpectedly, stearidonic acid (and derivatives

thereof) is useful in inhibiting the cyclooxygenase pathway. This enables stearidonic acid (and derivatives thereof) to be used for treating skin inflammation, particularly skin inflammation caused by radiation, such as UV radiation. Stearidonic acid is particularly useful in treating burns, particularly first degree burns such as sunburn;  
5 it can also be used prophylactically as part of a sunscreen compound.

Stearidonic acid (SA) is a polyunsaturated fatty acid of the n3 family; it is an essential fatty acid. Chemically it can be described as 6c9c12c15c-octadecatetraenoic acid or 18:4n3. Stearidonic acid can be formed in the human body by the desaturation of  $\alpha$ -linolenic acid (18:3n3) with the enzyme  $\Delta$ 6 desaturase.

10 There are occasions when the activity of this enzyme in the body may be too low to produce sufficient stearidonic acid. In these circumstances, compositions containing stearidonic acid may be taken as a dietary supplement. Stearidonic acid is known to inhibit the 5-lipoxygenase pathway and to moderate production of LTB<sub>4</sub> from leukocytes. However, it was not previously known that stearidonic acid would inhibit  
15 the cyclooxygenase pathway.

According to one aspect of the invention there is provided a sunscreen composition comprising stearidonic acid, or a physiologically acceptable derivative thereof, in combination with a UV blocking and/or UV absorbing material.

It is particularly preferred that the sun screen composition includes one  
20 or more of a moisturiser, an emollient, an emulsifier, a preservative, a dispersant, a viscosity modifier, a herbal extract, a solvent, a chelating agent, an antioxidant, a water-proofing agent, a pH adjuster, a perfume, and a protein.

It is particularly preferred that the sunscreen composition includes one or more of titanium dioxide; zinc oxide; benzophenone-3; benzophenone-4; octyl  
25 methoxycinnamate (Parsol 1789); 3,3,5-trimethylcyclohexyl salicylate; carbomer; hydroxyethyl cellulose; lanolin alcohols; cetyl phosphate; fatty alcohols; C<sub>12</sub> to C<sub>15</sub> alkyl benzoate; cyclomethicone; caprylic/capric triglycerides; mineral oil; glycerin; vitamin E; and isopropyl myristate.

The precise formulation of the sunscreen composition depends on the

form required for the composition. Broadly, it may be in the form of a solid or a liquid suitable for topical application. Typically, the composition is provided in the form of a cream, an emulsion or a gel; however, the composition may be provided in other forms, such as a solid stick.

5           According to another aspect of the invention, we provide a pharmaceutical composition for treating skin inflammation caused by burns, by exposure to sunlight or by exposure to UV radiation, comprising stearidonic acid, or a physiologically acceptable derivative thereof, and a physiologically acceptable carrier.

10           The carrier will include materials normally present in formulations for treating burns, such as an antiseptic compounds, emollients, inorganics, humectants, moisturisers, anti-inflammatory agents, vitamins, preservatives, pH adjusters, proteins, herbal extracts, carriers/solvents, soothing/cooling agents, antioxidants, perfumes, emulsifiers and viscosity modifiers. Specific examples of useful materials  
15 include glycerine, triethanolamine stearate, vitamin E, lanolin, zinc oxide, allantoin, calamine, sodium lactate, water, lactic acid, pro-vitamin B5 and menthol.

          The formulation of the carrier also depends on the form required for the pharmaceutical composition. Broadly, the pharmaceutical composition may be in the form of a solid or a liquid suitable for topical application. Typically, the  
20 pharmaceutical composition is provided in the form of a cream, an emulsion or a gel; however, the pharmaceutical composition may be provided in other forms, such as a solid stick.

          The amount of the stearidonic acid (or derivative) in the sunscreen composition or the pharmaceutical composition depends upon the way the  
25 composition is to be used. However, the compositions according to the invention typically contain 0.1 to 20 wt% of the stearidonic acid, or derivative, preferably 0.2 to 10 wt%.

          The compositions according to the invention may be provided in a bottle, a tube or any other suitable packaging. The container for the compositions

may be provided with dispensing means for dispensing the composition. Any known form of dispensing means may be used. When the composition is a liquid, it may be desirable to employ a dispensing means that can dispense the it in the form of a spray.

5                   Whilst any physiologically acceptable derivative of stearidonic acid may be used in the present invention, it is preferred that the derivative is an ester of stearidonic acid. More preferably the ester comprises an ester of stearidonic acid and an alcohol, particularly an ester of stearidonic acid and a polyol.

10                   It is particularly preferred that the derivative is the triglyceride of stearidonic acid. This triglyceride may be obtained from a number of sources. In one embodiment it can be extracted from seeds of the Borignaceae family, especially the genus "Echium". These seeds have been found to contain a rich source of stearidonic acid. This is described in greater detail in our copending PCT patent application of even date entitled "Vegetable Oil Composition".

15                   The compositions according to the invention may be incorporated in a wide variety of personal care or health care formulations.

                  According to another aspect of the invention there is provided the use of stearidonic acid, or a physiologically acceptable derivative thereof, in a sunscreen composition.

20                   According to another aspect of the invention there is provided the use of stearidonic acid, or a physiologically acceptable derivative thereof, for the manufacture of a medicament for treating skin inflammation caused by burns.

                  According to another aspect of the invention there is provided the use of stearidonic acid, or a physiologically acceptable derivative thereof, for the  
25                   manufacture of a medicament for treating skin inflammation caused by exposure to UV radiation, or by exposure to sunlight.

                  According to another aspect of the invention there is provided a method treating skin inflammation caused by burns, comprising topically applying stearidonic acid, or a physiologically acceptable derivative thereof, to an inflamed area.

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According to another aspect of the invention there is provided a method of treating skin inflammation caused by exposure to UV radiation or exposure to sunlight, comprising topically applying stearidonic acid, or a physiologically acceptable derivative thereof, to an inflamed area.

5           According to another aspect of the invention there is provided the use of stearidonic acid, or a physiologically acceptable derivative thereof, to inhibit the cyclooxygenase pathway.

          According to another aspect of the invention there is provided the use of stearidonic acid, or a physiologically acceptable derivative thereof, for the  
10   manufacture of a medicament for inhibiting the cyclooxygenase pathway.

Broadly the invention may be applied to treat skin irritation caused by overexposure to a wide variety of radiation , including UV radiation, infra red radiation, and radiation used during chemotherapy.

          The term "sunscreen composition" as used in this specification includes  
15   materials which substantially completely block UV radiation and includes material which only partially block UV radiation.

The following examples illustrate the invention.

#### Example 1

20           This example illustrates one way to make the triglyceride derivative of stearidonic acid. 10 kg of the seeds of echium plantagineum were crushed and the oil was extracted with 15 litres of petroleum ether (BP 40-60 °C). The petroleum ether extract was evaporated to yield 1741 g of a golden yellow oil. The oil was converted to the corresponding fatty acid methyl esters and was analysed by gas  
25   chromatography. The lipid profile was as follows:

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| <u>Fatty Acid</u> | <u>Fatty Acid Content</u> |
|-------------------|---------------------------|
| 16:0              | 7.2%                      |
| 18:0              | 4.0%                      |
| 18:1              | 18.2%                     |
| 18:2 (LA)         | 16.5%                     |
| 18:3 (GLA)        | 11.8%                     |
| 18:3 (ALA)        | 28.9%                     |
| 18:4 (SA)         | 12.2%                     |
| Other             | 1.2%                      |

### Example 2

This example illustrates another way to make the triglyceride derivative of stearidonic acid. 20 g of the seeds of *trichodesma zeylanicum* seeds were crushed and placed in a Soxhlet extraction thimble. An oil was isolated by refluxing n-hexane around the crushed seed to produce a solution of the oil in n-hexane. The oil was separated from the n-hexane by rotoevaporation; 5 g of a green oil was recovered.

An aliquot of the oil was converted to the corresponding fatty acid methyl esters and was analysed by gas chromatography. The lipid profile was as follows:

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|   | <u>Fatty Acid</u> | <u>Fatty Acid Content</u> |
|---|-------------------|---------------------------|
|   | 16:0              | 9.4%                      |
|   | 18:0              | 5.7%                      |
|   | 18:1              | 25.5%                     |
| 5 | 18:2 (LA)         | 19.0%                     |
|   | 18:3 (GLA)        | 5.5%                      |
|   | 18:3 (ALA)        | 26.5%                     |
|   | 18:4 (SA)         | 5.9%                      |
|   | Other             | 2.5%                      |

10

Example 3

Synthetic human skin grown from human fibroblasts has been demonstrated to be useful as a model for assessing phototoxicity. This model was used to evaluate the inhibiting action of topically applied lipids.

Duplicate 9 x 9 mm Model ZK1301 tissues (obtainable from Advanced Tissue Sciences, La Jolla, California, USA) were dosed with 3 microlitres of test oil. Control tissues were untreated. The test oils were: blackcurrant seed oil; borage seed oil (this is a boragnaceae oil with no stearidonic acid); marine oil; the oil from Example 1; and the oil from Example 2. The tissues were incubated for 24 hours at 37°C in an atmosphere with 5% CO<sub>2</sub> and greater than 90% humidity. Half the tissues were then exposed to 4 J/cm<sup>2</sup> UVB radiation using a Dr Honle Solar simulator to stimulate the inflammatory response.

The tissues were then incubated for a further 24 hours. The tissue supernatants were collected and the tissues were evaluated for cell viability by an MTT (3(4,5-dimethyl thiazol-2-yl) 2,5-diphenyl tetrazolin bromide) dye reduction assay, using the Skin MTT Assay Kit ZA0022 (available from Advanced Tissue Sciences, La Jolla, California, USA). This protocol is based on a published method (T. Mosmann, J.Immunol. Meth., 65 55 (1983)).

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A PGE<sub>2</sub> assay was performed on the supernatants. PGE<sub>2</sub> is a strongly proinflammatory eicosanoid; its release is indicative of membrane perturbation events that activate phospholipase A<sub>2</sub> to release arachidonic acid. Arachidonic acid is the precursor to PGE<sub>2</sub> via . The PGE<sub>2</sub> assay on the supernatant was carried out using a  
 5 PGE<sub>2</sub> assay kit ZA0050, method number 6-FRD0019/Rev 002 (available from Advanced Tissue Sciences, La Jolla, California, USA). This method has been described by E. Granstrom et al in Prostaglandin Thrombox. Res. 5 119 (1978).

The results of the MTT Assay were as follows:

| 10 | <u>Test Material</u>  | <u>Mean MTT Optical Density</u> |            |
|----|-----------------------|---------------------------------|------------|
|    |                       | <u>No UVB</u>                   | <u>UVB</u> |
|    | Control               | 1.52                            | 1.25       |
|    | Blackcurrant seed oil | 2.54                            | 1.30       |
|    | Borage seed oil       | 1.63                            | 1.39       |
| 15 | Marine Oil            | 1.45                            | 1.27       |
|    | Oil from Example 1    | 1.47                            | 1.36       |
|    | Oil from Example 2    | 1.53                            | 1.45       |

None of these materials produced any notable cytotoxicity or  
 20 phototoxicity.

The results of the PGE<sub>2</sub> assay were as follows:

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| <u>Test Material</u>  | <u>Mean PGE<sub>2</sub> Release (pg/ml)</u> |            |
|-----------------------|---------------------------------------------|------------|
|                       | <u>No UVB</u>                               | <u>UVB</u> |
| Control               | 1300                                        | 17000      |
| Blackcurrant seed oil | 5100                                        | 15000      |
| 5 Borage seed oil     | 1400                                        | 16000      |
| Marine Oil            | 3100                                        | 19000      |
| Oil from Example 1    | 2400                                        | 8100       |
| Oil from Example 2    | 2100                                        | 9600       |

10                    These results demonstrate that UVB irradiation of control tissue caused a 13 fold increase in release of PGE<sub>2</sub>. Preincubation with the oil from Examples 1 and 2 blocked this by 50%.

                      It will be seen that the oils from Example 1 and 2 are much more effective than blackcurrant seed oil. The main difference between the blackcurrant  
 15 seed oil is that it has much less stearidonic acid than the oils in Example 1 and 2 (typically blackcurrant seed oil contain 3 to 4 wt% of stearidonic acid).

#### Example 4

A sunscreen oil was prepared from the following ingredients:

20

|                                                      |              |
|------------------------------------------------------|--------------|
| Butyl methoxydibenzoyl methane (Parsol 1789)(1)      | 2.0 wt%      |
| Octyl methoxycinnamate (Parsol MCX)(1)               | 7.5 wt%      |
| Benzophenone-3 (Uvinul M40)(2)                       | 4.5 wt%.     |
| PPG-2 myristyl ether propionate (Promyristyl PM3)(3) | 10.0 wt%     |
| 25 Oil from Example 1                                | 2.0-10.0 wt% |
| Caprylic/capric triglycerides (Crodamol GTCC)        | to 100 wt%   |
| Perfume, preservatives, colour                       | qs           |
| (1) From Givaudan                                    |              |
| (2) From BASF                                        |              |

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(3) From Croda

The sunscreen oil was formed by blending the ingredients, heating gently. The resultant blend was stirred to cool.

5

Example 5

A physical block sunscreen cream was prepared from the following ingredients:

10

## Oil Phase:

|    |                                                      |              |
|----|------------------------------------------------------|--------------|
|    | Myristyl myristate (Crodamol MM)(1)                  | 1.5 wt%      |
|    | Dimethicone (silicone 200/200)(2)                    | 7.0 wt%      |
|    | Glyceryl stearate (GMS N/E DP2186)(1)                | 2.5 wt%      |
| 15 | Stearic acid (Crosterene SA4130)(1)                  | 3.0 wt%      |
|    | PVP/eicosene copolymer (Antaron V220)(3)             | 0.5 wt%      |
|    | Nonionic emulsifying blend (Polawax GP200 DP2307)(1) | 2.0 wt%      |
|    | Octyl hydroxy stearate (Crodamol OHS)(1)             | 5.0 wt%      |
|    | Oil from Example 1                                   | 2.0-10.0 wt% |
| 20 | Super refined shea butter(1)                         | 5.0 wt%      |
|    | Caprylic/capric triglycerides (Crodamol GTCC)(1)     | 9.0 wt%      |
|    | Titanium dioxide                                     | 5.0 wt%      |

## Water Phase:

|    |                                |            |
|----|--------------------------------|------------|
| 25 | Deionised water                | to 100 wt% |
|    | Flobeads (CL-2080)(5)          | 5.0 wt%    |
|    | Glycerine                      | 3.0 wt%    |
|    | Triethanolamine                | 0.9 wt%    |
|    | Perfume, preservatives, colour | qs         |

- (1) From Croda
- (2) From Dow Corning
- (3) From GAF
- (4) From K&K Greif
- 5 (5) From Landsdowne Chemicals

The sunscreen cream was made by heating the oil phase (including titanium dioxide) and water phase separately to 80-85°C, then adding the water phase to the oil phase with vigorous agitation. The triethanolamine was then added.

10 At 45°C the Flobeads were added. The stirring was continued until the temperature reached about 55°C, and then the composition was passed through suitable homogenising equipment, such as a triple roll mill).

#### Example 6

15

An antioxidant cream was prepared from the following ingredients:

#### Oil Phase:

|    |                                                    |          |
|----|----------------------------------------------------|----------|
|    | Cosmowax D (cetearyl alcohol (and) Cetearyl 20)(1) | 2.10 wt% |
|    | Crillet 3 (Polysorbate 60)(1)                      | 2.50 wt% |
| 20 | Crodacol C90 (cetyl alcohol)(1)                    | 2.50 wt% |
|    | Crodamol GTCC (capric/caprylic triglycerides)(1)   | 7.50 wt% |
|    | Vitamin E (2)                                      | 0.50 wt% |
|    | Ascorbyl palmitate (2)                             | 0.20 wt% |
|    | SR Echium Oil (1)                                  | 2.00 wt% |

25

#### Water Phase:

|  |                                              |            |
|--|----------------------------------------------|------------|
|  | Cellose QP30000H (hydroxyethyl cellulose)(3) | 0.50 wt%   |
|  | Croderol GA7000 (Glycerin)(1)                | 2.00 wt%   |
|  | Deionised water                              | to 100 wt% |

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Perfume, preservative, colour

qs

(1) From Croda

(2) From Roche

5 (3) From Union Carbide

The oil and water phases are heated separately to 65-70°C, then the water phase is added to the oil phase while stirring. The composition is then stirred to cool.

10

Example 7

A cooling aftersun cream was prepared from the following ingredients:

## Oil Phase:

|    |                                                               |          |
|----|---------------------------------------------------------------|----------|
| 15 | Crodamol IPM (isopropyl stearate)(1)                          | 5.00 wt% |
|    | Crodamol CAP (cetearyl octanoate)(1)                          | 2.00 wt% |
|    | SR Trichodesma Oil(1)                                         | 2.00 wt% |
|    | Polawax GP200 (nonionic emulsifying wax)(1)                   | 2.00 wt% |
|    | Cithrol GMS A/S (Glyceryl stearate (and) PEG-100 stearate)(1) | 3.00 wt% |
| 20 | Silicone Fluid 200/100 cs (dimethicone)(2)                    | 0.50 wt% |
|    | Menthol                                                       | 0.10 wt% |
|    | Allantoin                                                     | 0.25 wt% |

## Water Phase:

|    |                                |           |
|----|--------------------------------|-----------|
| 25 | Carbopol 934 (Carbomer 934)(3) | 0.25 wt%  |
|    | Ethanol DEB100                 | 2.00 wt%  |
|    | Triethanolamine 99%            | to pH 6.5 |
|    | Deionised water                | to 100%   |
|    | Perfume, preservative, colour  | qs        |

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- (1) From Croda
- (2) From Dow Corning
- (3) From B F Goodrich

- 5 The carbopol should first be hydrated in water at about 60-65°C, then the remaining water-phase ingredients should be added. Both phases should then be heated to 65-70°C, and then the water phase should be added to the oil phase whilst stirring. Finally, the composition should be neutralised with the amine and stirred to cool.

#### 10 Example 8

A calamine cream was prepared from the following ingredients:

##### Oil Phase:

|    |                                                  |          |
|----|--------------------------------------------------|----------|
|    | Polawax GP200 (nonionic emulsifying wax)(1)      | 8.00 wt% |
| 15 | Crillet 3 (Polysorbate 60)(1)                    | 1.00 wt% |
|    | SR Trichodesma oil(1)                            | 2.00 wt% |
|    | Crodamol GTCC (capric/caprylic triglycerides)(1) | 3.00 wt% |

##### Water Phase:

|    |                               |            |
|----|-------------------------------|------------|
| 20 | Distilled Witch Hazel         | 10.00 wt%  |
|    | Croderol GA7000(1)            | 5.00 wt%   |
|    | Zinc oxide                    | 2.00 wt%   |
|    | Calamine                      | 2.00 wt%   |
|    | Deionised water               | to 100 wt% |
| 25 | Perfume, preservative, colour | qs         |

The oil and water phases are heated separately to 65-70°C. The two phases are then combined while stirring. The zinc oxide and calamine are then added under high shear. Finally, the composition is stirred to cool.

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Whilst certain embodiments of the invention have been described above, it will be appreciated that modifications can be made.

CLAIMS

1. A sunscreen composition comprising stearidonic acid, or a physiologically acceptable derivative thereof, in combination with a UV blocking and/or UV  
5 absorbing material.
2. A composition according to claim 1, comprising one or more of a moisturiser, an emollient, an emulsifier, a preservative, a dispersant, a viscosity modifier, a herbal extract, a solvent, a chelating agent, an antioxidant, a water-proofing agent, a pH  
10 adjuster, a perfume, and a protein.
3. A composition according to claim 2, comprising one or more of titanium dioxide; zinc oxide; benzophenone-3; benzophenone-4; octyl methoxycinnamate (Parsol 1789); 3,3,5-trimethylcyclohexyl salicylate; carbomer; hydroxyethyl cellulose;  
15 lanolin alcohols; cetyl phosphate; fatty alcohols; C<sub>12</sub> to C<sub>18</sub> alkyl benzoate; cyclomethicone; caprylic/capric triglycerides; mineral oil; glycerin; vitamin E; and isopropyl myristate.
4. A composition according to claim 1, 2 or 3, comprising 0.1 to 20 wt% of the  
20 stearidonic acid, or derivative.
5. A composition according to any preceding claim, comprising 0.2 to 10 wt% of the stearidonic acid, or derivative.
- 25 6. A composition according to any preceding claim, wherein the derivative of stearidonic acid comprises the triglyceride derivative of stearidonic acid.
7. A composition according to any preceding claim, wherein the derivative of stearidonic acid comprises an oil extracted from seeds of the Boraginaceae family.

8. The use of stearidonic acid, or a physiologically acceptable derivative thereof, in a sunscreen composition.

9. The use of stearidonic acid, or a physiologically acceptable derivative thereof,  
5 for the manufacture of a medicament for treating skin inflammation caused by burns.

10. The use of stearidonic acid, or a physiologically acceptable derivative thereof, for the manufacture of a medicament for treating skin inflammation caused by exposure to UV radiation, or by exposure to sunlight.

10

11. A method of treating skin inflammation caused by burns, comprising topically applying stearidonic acid, or a physiologically acceptable derivative thereof, to an inflamed area.

15 12. A method of treating skin inflammation caused by exposure to UV radiation or exposure to sunlight, comprising topically applying stearidonic acid, or a physiologically acceptable derivative thereof, to an inflamed area.

13. The use of stearidonic acid, or a physiologically acceptable derivative thereof,  
20 to inhibit the cyclooxygenase pathway.

14. The use of stearidonic acid, or a physiologically acceptable derivative thereof, for the manufacture of a medicament for inhibiting the cyclooxygenase pathway.

25 15. A pharmaceutical composition for treating skin inflammation caused by burns, by exposure to sunlight or by exposure to UV radiation, comprising stearidonic acid, or a physiologically acceptable derivative thereof, and a physiologically acceptable carrier.

16. A pharmaceutical composition according to claim 15, wherein the carrier includes a soothing/cooling agent.

17. A pharmaceutical composition according to claim 15 or 16, wherein the carrier includes one or more of an antiseptic compound, an emollient, an inorganic, a humectant, a moisturiser, an anti-inflammatory agent, a vitamin, a preservative, a pH adjuster, a protein, a herbal extract, a carriers/solvent, an antioxidant, a perfume, an emulsifier and a viscosity modifier

18. A pharmaceutical composition according to claim 15, 16 or 17, wherein the carrier includes one or more of glycerine, triethanolamine stearate, vitamin E, lanolin, zinc oxide, allantoin, calamine, sodium lactate, water, lactic acid, pro-vitamin B5 and menthol.

19. A pharmaceutical composition according to any one of claims 15 to 18, containing 0.1 to 20 wt% of the stearidonic acid, or derivative.

20. A pharmaceutical composition according to any one of claims 15 to 18, containing 0.2 to 10 wt% of the stearidonic acid, or derivative.

21. A composition according to any one of claims 15 to 20, wherein the derivative of stearidonic acid comprises the triglyceride derivative of stearidonic acid.

22. A composition according to any one of claims 15 to 21, wherein the derivative of stearidonic acid comprises an oil extracted from seeds of the Borignaceae family.

# INTERNATIONAL SEARCH REPORT

Intern. Appl. Application No

PCT/GB 97/01496

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 6 A61K7/48 A61K31/20 A61K31/23

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61K

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

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

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages                                                                                    | Relevant to claim No. |
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| X          | US 5 178 873 A (HORROBIN DAVID F ET AL)<br>12 January 1993<br>see column 2, line 40 - column 4, line 68<br>see claims 1-4<br>---                                      | 13,14                 |
| X          | WO 94 15464 A (ABBOTT LAB) 21 July 1994<br>see page 13, last paragraph<br>see examples I,II<br>see claims 1,2,4,7,9,10,17<br>---                                      | 13,14                 |
| Y          | FR 2 648 347 A (SEDERMA SA) 21 December 1990<br>see page 1, line 1 - page 2, line 29<br>see page 3, line 15 - page 4, line 23<br>see claims 1-3,6-8,10<br>---<br>-/-- | 1-3,6-12              |



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

### \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
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- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

"I" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\* & \* document member of the same patent family

Date of the actual completion of the international search

12 September 1997

Date of mailing of the international search report

01.10.97

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# INTERNATIONAL SEARCH REPORT

Intern. Application No  
PCT/GB 97/01496

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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# INTERNATIONAL SEARCH REPORT

International application No. -

PCT/GB 97/ 01496

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
  
Please see Further Information sheet enclosed
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

**FURTHER INFORMATION CONTINUED FROM PCT/ISA210**

Remark: Although claims 11-12 are directed to a method of treatment of (diagnostic method practised on) the human/animal body the search has been carried out and based on the alleged effects of the compound/composition.

# INTERNATIONAL SEARCH REPORT

information on patent family members

International Application No

PCT/GB 97/01496

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information on patent family members

Inter. Application No

PCT/GB 97/01496

| Patent document<br>cited in search report | Publication<br>date | Patent family<br>member(s) | Publication<br>date |
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