**USE OF ZINC SALTS OF CONJUGATED LINOLEIC ACIDS TO TREAT SKIN DISORDERS**

**VERWENDUNG VON ZINKSALZEN DER KONJUGIERTEN LINOLEINSÄUREN ZUR BEHANDLUNG VON HAUTKRANKHEITEN**

**UTILISATION DES SELS DE ZINC D’ACIDES LINOLEIQUES CONJUGUES POUR LE TRAITEMENT DES MALADIES DE LA PEAU**

**References cited:**

- DATABASE WPI Week 9507 Derwent Publications Ltd., London, GB; AN 95-044024 XP002053010 & CZ 9 300 924 A (STOL) , 15 December 1994

**Remarks:**
The file contains technical information submitted after the application was filed and not included in this specification.

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Description


[0002] Conjugated linoleic acid and linoleic acid are well-known for their therapeutic, particularly chemotherapeutic, properties (see, for example, Belury, M.A., 1995 Nutrition Reviews, 53 (4) : 83-39 and references therein; Pariza, M.W., Chemistry & Industry, 16 June 1997, 464-466; EP 0 087 863; EP 0 044 314; EP 0 078 434; EP 0 003 407; EP 0 057 175; EP 0 071 357; EP 0 085 579; EP 0 139 480), and have comprised non-essential components of compositions for treating skin disorders (EP 0 727 991). WO 95/13806 discloses the use of a composition comprising zinc salts of 68% (unconjugated) linoleic acid and 10% conjugated isomers of linoleic acid for use in treating skin disorders.

[0003] However, the present inventor has now found that zinc salts of conjugated linoleic acids have an unexpectedly great efficacy in the treatment of skin disorders when compared to for example unconjugated zinc linoleate.

[0004] According to the present invention, there is provided the use of a composition comprising the zinc salt of at least one conjugated linoleic acid in the manufacture of a medicament comprising at least 50% w/w said zinc salt for treating skin disorders. The composition may be used in a method of treating skin disorders.

[0005] Methods of manufacture and use of the compositions and medicaments of the present invention will be readily apparent to one skilled in the art and are exemplified in the Examples below.

[0006] The medicament may comprise at least 50%, for example at least 60%, 70%, 80% or 90%, the zinc salt of at least one conjugated linoleic acid. For example it may substantially comprise the zinc salt of a conjugated linoleic acid or it may comprise a substantially greater proportion of the zinc salt or salts of at least one conjugated linoleic acid than of zinc linoleate.

[0007] The present inventor has found that the zinc salts of conjugated linoleic acids have a surprisingly great efficacy, compared to that of conjugated linoleic acids alone (which may act as irritants) and of zinc linoleate, when used in the treatment and/or prophylaxis of skin disorders such as eczema, psoriasis, cold sores (herpes) and dermatitis.

[0008] The conjugated linoleic acids are a large family of molecules. Dienoic conjugated linoleic acids may be used as the basis of the zinc salts of the present invention. For example, 9,11-octadecadienoic acid or 10,12-octadecadienoic acid may be used. These unsaturated molecules contain double bonds and so there are a number of geometric isomes of the molecules, for example cis9,trans11-octadecadienoic acid and trans9,cis11-octadecadienoic acid.

[0009] The medicament of the present invention may be used in conjunction with a pharmaceutically acceptable carrier, diluent or excipient. Such carriers, diluents and excipients are well known - see for example Remington's Pharmaceutical Sciences and US Pharmacopeia (1984) Mack Publishing Company, Easton, PA.

[0010] The medicament may also comprise at least one antioxidant, for example tocopherol (Vitamin E).

[0011] The medicament may also comprise for example zinc linoleate and/or the zinc salt of at least one other fatty acid. Conjugated linoleic acids are usually prepared by the isomerisation of linoleic acid, and are therefore liable to contain various residues of linoleic acid. Thus zinc linoleate may be among the zinc salts formed when the isomerised linoleic acid is converted into zinc salts.

[0012] The zinc salts of conjugated linoleic acids appear to be more effective than zinc salts of other fatty acids, and (see examples B and C below) do not owe their activity to the presence of zinc alone.

[0013] Medicaments and compositions according to the present invention may be administered in doses (i.e. concentrations and quantities) sufficient to effect the desired prophylactic or therapeutic result. Such doses may be readily determined using simple dose-response experiments.

[0014] The doses may be such that they are substantially non-irritant to the patient.

[0015] According to a further aspect of the present invention, there is provided the use of a composition comprising substantially the zinc salt of at least one conjugated linoleic acid in the manufacture of a medicament for treating cancer. The composition may be used in a method of treating cancer.

[0016] Methods of manufacture and use of the compositions and medicaments of the present invention will be readily apparent to one skilled in the art, particularly with reference to the Examples below.

[0017] The composition may comprise at least 50%, for example at least 60%, 70%, 80% or 90%, the zinc salt of at least one conjugated linoleic acid. For example it may substantially comprise the zinc salt of a conjugated linoleic acid or it may comprise a substantially greater proportion of the zinc salt or salts of at least one conjugated linoleic acid than of zinc linoleate.

[0018] A zinc salt may for example be of 9,11-octadecadienoic acid or 10,12-octadecadienoic acid.

[0019] The zinc salts of the compositions of the present invention for the treatment and/or prophylaxis of skin disorders also appear to be useful in the treatment and/or prophylaxis of cancer, particularly epidermal cancers such as skin cancer.

[0020] The medicament may additionally comprising a pharmaceutically acceptable carrier, diluent or excipient.

[0021] The invention will be further apparent from the following description and examples which show, by way of example only, zinc salts of conjugated linoleic acids for use in the treatment of skin disorders.
Example A

[0022] Preparation of zinc conjugated linoleates (ZCL) in a formulation suitable for topical application.

[0023] 215g of Pamolyn (RTM) 380 (Hercules Inc., Hercules Plaza, Wilmington, DE 19894, USA) containing ca. 69% of conjugated linoleic acids was heated to 70°C with 500g Emulsifying Ointment BP: 32.5g of zinc oxide was added slowly with stirring. Heating was continued for a further 5 minutes, then 1,250ml of boiling demineralised water was slowly added with stirring. The whole hot product was then emulsified by vigorous mechanical agitation and allowed to cool, giving a white semi-cream which when cool was well absorbed on topical application to the skin with gentle rubbing.

[0024] The physical characteristics of the product were varied by increasing or decreasing the proportion of water during the preparation. One half of the above proportion of water gave an ointment, whereas increasing the proportion of water by 50% gave a cream.

Example B

[0025] A male patient suffering from eczema, mainly on the arms, was treated by daily topical application of the ZCL semi-cream of Example A. The condition was completely cured within 4 days.

Example C

[0026] Previous treatment as in Example B with a product similar to that of Example A but containing only one-seventh of the proportion of ZCL, but the same proportion of zinc, had improved the eczema to a limited extent but had not provided a complete cure even after application over 2 weeks.

Example D

[0027] The product prepared as in Example A was used to treat a female patient suffering from facial psoriasis. This condition was greatly improved within 1 day and essentially cured within 2 days.

Example E

[0028] A male patient aged 70 years suffering from pruritus of the legs and scalp was treated by topical application of a semi-cream prepared as in Example A. Itching ceased within 10-15 minutes.

Example F


Example G

[0030] A female patient of 55 years age suffered severe discomfort caused by pressure sores on the trunk. A single application of the semi-cream of Example A rapidly alleviated all soreness and discomfort.

Example H

[0031] A male patient of 55 years age suffered from an erupted (i.e. broken skin) cold sore (Herpes). Treatment with the semi-cream of Example A rapidly removed the soreness and discomfort, and the condition was essentially cured within 2 days.

Example I

[0032] A male patient suffering from skin cancer applied the semi-cream of Example A on a daily basis to an area of skin cancer. Over a period of four months, the appearance of the affected area improved (although the cancer did not totally disappear) and itching of the affected area stopped. Discontinuation of treatment resulted in the recurrence of itching at the affected area.

Example J

[0033] A female patient had a patch of discoloured skin on one ankle which was medically diagnosed as skin cancer. Application to the affected area of the semi-cream of Example A completely stopped unpleasant itching felt at the affected area. Continued use over a period of about six months resulted in the patch of cancerous skin becoming much less raw in appearance and it started to break up into islets separated by skin of more normal appearance.

Claims

1. The use of a composition comprising the zinc salt of at least one conjugated linoleic acid in the manufacture of a medicament comprising at least 50% w/w said zinc salt for treating skin disorders.

2. The use according to claim 1, the medicament comprising at least 60%, 70%, 80%, or 90% w/w the zinc salt of at least one conjugated linoleic acid.

3. The use according to either one of the preceding claims, a conjugated linoleic acid being selected from the group of 9,11-octadecadienoic acid and 10,12-octadecadienoic acid.

4. The use according to any one of the preceding claims, the skin disorder being selected from any one of the group of eczema, psoriasis, cold sores and dermatitis.
5. The use of a composition comprising substantially the zinc salt of at least one conjugated linoleic acid in the manufacture of a medicament for treating cancer.

6. The use according to claim 5, the composition comprising at least 50% w/w the zinc salt of at least one conjugated linoleic acid.

7. The use according to claim 6, the composition comprising at least 60%, 70%, 80%, or 90% w/w the zinc salt of at least one conjugated linoleic acid.

8. The use according to any of claims 5-7, a conjugated linoleic acid being selected from the group of 9,11-octadecadienoic acid and 10,12 octadecadienoic acid.

9. The use according to either of claims 7 or 8, the cancer being skin cancer.

Patentansprüche


8. Verwendung nach einer der Ansprüche 5 bis 7, dadurch gekennzeichnet, dass die konjugierte Linolsäure ausgewählt ist aus der Gruppe von 9,11-Octadecadiensäure und 10,12-Octadecadiensäure.

9. Verwendung nach einem der Ansprüche 7 oder 8, dadurch gekennzeichnet, dass der Krebs Hautkrebs ist.

Revendications

1. Utilisation d'une composition comprenant le sel de zinc d'au moins un acide linoléique conjugué dans la fabrication d'un médicament comprenant au moins 50 % m/m dudit sel de zinc pour traiter des maladies de la peau.

2. Utilisation selon la revendication 1, le médicament comprenant au moins 60 %, 70 %, 80 % ou 90 % m/m du sel de zinc d'au moins un acide linoléique conjugué.

3. Utilisation selon l'une quelconque des revendications précédentes, un acide linoléique conjugué étant choisi dans le groupe constitué de l’acide 9,11-octadécadiénique et l’acide 10,12-octadécadiénique.

4. Utilisation selon l'une quelconque des revendications précédentes, la maladie de la peau étant choisie dans le groupe constitué de l’eczéma, le psoriasis, l’herpès labial et la dermite.

5. Utilisation d'une composition comprenant substantiellement le sel de zinc d'au moins un acide linoléique conjugué dans la fabrication d'un médicament pour traiter le cancer.

6. Utilisation selon la revendication 5, la composition comprenant au moins 50 % m/m du sel de zinc d'au moins un acide linoléique conjugué.

7. Utilisation selon la revendication 6, la composition comprenant au moins 60 %, 70 %, 80 % ou 90 % m/m du sel de zinc d'au moins un acide linoléique conjugué.

8. Utilisation selon l’une quelconque des revendications 5 à 7, un acide linoléique conjugué étant choisi dans le groupe constitué de l’acide 9,11-octadécadiénique et l’acide 10,12-octadécadiénique.
9. Utilisation selon l'une quelconque des revendications 7 ou 8, le cancer étant le cancer de la peau.