



No. 06-128572- -00005-0000

Fecha: 2008-07-21 16:27:25 Dep. 2020 NUECREACIONE
Tra. 11 PATENTEIYII Eve: 379 FASENACIONALII
Act. 329 CTOINFORMACION Folios: 6**FORMULARIO UNICO DE COR**

1	SOLICITUD DE: ☐ Corrección de Error Material ☒ Modificación a una solicitud	
2 SOLICITANTE	Nombre: BIRKEN GMBH Sociedad constituida y existente bajo las leyes de Alemania. Dirección: Streiflingsweg 11 75223 Niefern-Öschelbronn, Alemania Domicilio: Niefern-Öschelbronn, Alemania Teléfono: 546 09 70 Fax: 249 40 70 E-mail: clientes@camyp.com	IDENTIFICACION C.C. ☐ NIT ☐ C.E. ☐ Otro ☐ Número: _____
3 REPRESENTANTE O APODERADO	Nombre: Emilio FERRERO Dirección: Carrera 4ª No. 72-35 Teléfono: 347 36 11 Fax: 217 92 11 E-mail: cavelier@cavelier.com	IDENTIFICACION C.C. ☒ NIT ☐ C.E. ☐ Otro ☐ Número: 438.019 TP 31.929
4	Número de expediente: 06.128.572	
5	Descripción de la corrección o modificación solicitada: Presento nuevo capítulo reivindicatorio compuesto por 30 reivindicaciones y solicito atentamente que el examen de patentabilidad sea realizado sobre éste.	
6	Comprobante de pago No. 08-53.610 Fecha: 7 de julio de 2008	
7	Anexos ☒ Comprobante de pago de la tasa por \$103.000, por concepto de modificaciones. ☐ Poderes, si fuere el caso ☐ Documento que acredita la existencia y representación legal de las partes, cuando sean personas jurídicas.	
8	NOMBRE: EMILIO FERRERO FIRMA:  C.C. 438.019 de Usaquén T.P.A. 31.929	

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REIVINDICACIONES

1. Un oleogel que comprende:

5 - un líquido no polar que tiene una fracción entre 80 y 99%
en peso, con base en el peso total del gel,
-por lo menos un triterpeno altamente dispersado que tiene un
tamaño de partícula promedio menor a 50 μm como un agente
formador de oleogel en una fracción entre 1% en peso y 20% en
10 peso, con base en el peso total del gel.

2. El oleogel de acuerdo con la reivindicación 1,
donde el tamaño de partícula promedio del al menos un
triterpeno es menor a 10 μm .

15 3. El oleogel de acuerdo con las reivindicaciones 1 ó 2,
donde la fracción de aglomerados secundarios del al menos un
triterpeno es menor a 20% en peso.

20 4. El oleogel de acuerdo con cualquiera de las reivindicaciones 1
a 3,
donde el al menos un triterpeno tiene una distribución de
tamaño de partícula homogénea.

25 5. El oleogel de acuerdo con cualquiera de las reivindicaciones 1
a 4,
donde el área de superficie específica del al menos un
triterpeno está entre 1 m^2/g y 500 m^2/g .

30 6. El oleogel de acuerdo con la reivindicación 5,
donde el área de superficie específica del al menos un
triterpeno está entre 10 m^2/g y 100 m^2/g .

35 7. El oleogel de acuerdo con la reivindicación 6,
donde el área de superficie específica del al menos un
triterpeno está entre 20 m^2/g y 50 m^2/g .

40 8. El oleogel de acuerdo con cualquiera de las reivindicaciones 1
a 7,
donde la fracción del al menos un triterpeno altamente
dispersado es mayor a 80% en peso.

9. El oleogel de acuerdo con la reivindicación 8,
donde la fracción del al menos un triterpeno altamente
dispersado es mayor a 90% en peso.

5 10. El oleogel de acuerdo con cualquiera de las reivindicaciones 1
a 9,
donde el al menos un triterpeno tiene una fracción de más de
80% en peso de betulina.

10 11. El oleogel de acuerdo con cualquiera de las reivindicaciones 1
a 10,
donde la fracción del agente formador de oleogel está entre
3% en peso y 15% en peso.

15 12. El oleogel de acuerdo con la reivindicación 11,
donde la fracción de líquido no polar está entre 88% en peso
y 94% en peso y la fracción del agente formador de oleogel
está entre 6% en peso y 12% en peso.

20 13. El oleogel de acuerdo con cualquiera de las reivindicaciones 1
a 12,
donde el líquido no polar es aceite vegetal, animal, mineral
o sintético.

25 14. El oleogel de acuerdo con la reivindicación 13,
donde el aceite es uno de los siguientes aceites vegetales:
aceite de girasol, aceite de oliva, aceite de aguacate,
aceite de almendra o una mezcla de los mismos.

30 15. El oleogel de acuerdo con cualquiera de las reivindicaciones 1
a 12,
donde el líquido no polar es una cera o una parafina.

35 16. Un método para la producción de un oleogel, que comprende una
mezcla de los siguientes ingredientes:

- un líquido no polar en una fracción entre 80% en peso y 99%
en peso, con base en el peso total del gel,
-al menos un triterpeno altamente dispersado que tiene un
40 tamaño de partícula promedio menor a 50 μm como un agente
formador de oleogel en una fracción entre 1% en peso y 20% en
peso, con base en el peso total del gel.

17. El método de acuerdo con la reivindicación 16,
donde el tamaño de partícula promedio del al menos un
triterpeno es menor a 10 μm .

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18. El método de acuerdo con las reivindicaciones 16 ó 17,
donde la fracción de aglomerados secundarios del al menos un
triterpeno es menor a 20% en peso.

10 19. El método de acuerdo con cualquiera de las reivindicaciones 16
a 18,

donde el al menos un triterpeno tiene una distribución de
tamaño de partícula homogénea.

15 20. El método de acuerdo con cualquiera de las reivindicaciones 16
a 19,

donde el área de superficie específica del al menos un
triterpeno está entre 1 m^2/g y 500 m^2/g .

20 21. El método de acuerdo con la reivindicación 20,
donde el área de superficie específica del al menos un
triterpeno está entre 10 m^2/g y 100 m^2/g .

22. El método de acuerdo con la reivindicación 21,
25 donde el área de superficie específica del al menos un
triterpeno está entre 20 m^2/g y 50 m^2/g .

23. El método de acuerdo con cualquiera de las reivindicaciones 16
a 22,

30 donde la fracción del al menos un triterpeno altamente
dispersado es mayor a 80% en peso.

24. El método de acuerdo con la reivindicación 23,
donde la fracción del al menos un triterpeno altamente
35 dispersado es mayor a 90% en peso.

25. El método de acuerdo con cualquiera de las reivindicaciones 16
a 24,

40 donde el al menos un triterpeno tiene una fracción de más de
80% en peso de betulina.

26. El método de acuerdo con cualquiera de las reivindicaciones 16 a 25,

donde la fracción del agente formador de oleogel está entre 3% en peso y 15% en peso.

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27. El método de acuerdo con la reivindicación 26,

donde la fracción de líquido no polar está entre 88% en peso y 94% en peso y la fracción del agente formador de oleogel está entre 6% en peso y 12% en peso.

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28. El método de acuerdo con cualquiera de las reivindicaciones 16 a 27,

donde el líquido no polar es aceite vegetal, animal, mineral o sintético.

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29. El método de acuerdo con la reivindicación 28,

donde el aceite es uno de los siguientes aceites vegetales: aceite de girasol, aceite de oliva, aceite de aguacate, aceite de almendra o una mezcla de los mismos.

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30. El método de acuerdo con cualquiera de las reivindicaciones 16 a 27,

donde el líquido no polar es una cera o una parafina.

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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

NIT : 800174089-2

RECIBO OFICIAL DE CAJA : 08 - 53,610
FECHA : JULIO 7 DE 2008

***** CONSIGNACION *****

DEPOSITANTE	TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PGO	Vr. PAGO
CAVELIER ABOGADOS	CONSIGNACION	BANCO DE BOGOTA	042754387	664061	07/07/2008	21,445,000.00

***** CONCEPTO *****

CONCEPTO	CONCEPTO	TOTAL CONCEPTO
1 50005-01-03 CAMBIO DE MODALIDAD Y MODIFICA	12 MARCAS Y LENAS COMERCIALES	103,000.00
TOTAL :		\$ 103,000.00

SON: CIENTO TRES MIL PESOS

RESPONSABLE :

RECIBO DE CASH APLICADO AL EXPEDIENTE No.

010 15695-891-001-1

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BT



Industria y Comercio
SUPERINTENDENCIA

DIVISIÓN DE NUEVAS CREACIONES

RADICACIÓN EXPEDIENTE No. 06-128572

EL EXTRACTO DE LA PRESENTE SOLICITUD DE PATENTE DE INVENCION

FUE PUBLICADO EN LA GACETA DE PROPIEDAD INDUSTRIAL No 583 DE

FECHA 18 DE DICIEMBRE DE 2007 EL TÉRMINO HÁBIL SEÑALADO POR LA

LEY EXPIRA EL 14 DE MARZO DE 2008

NOTA: Dentro del plazo de los seis (6) meses siguientes a partir de la fecha de publicación en la gaceta de Propiedad Industrial, deberá solicitar y cancelar el examen de patentabilidad so pena de que la solicitud caiga en abandono, de acuerdo con lo establecido en el Artículo 44 de la Decisión 486/2000.

SE PRESENTARON OPOSICIONES POR PARTE DE TERCEROS.

SI _____

NO X



US 20030087789A1

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76(19) **United States**(12) **Patent Application Publication** (10) **Pub. No.: US 2003/0087789 A1**
Scheffler (43) **Pub. Date: May 8, 2003**(54) **EMULSION CONTAINING A PLANT
EXTRACT, METHOD FOR PRODUCING
SAID EMULSION AND FOR OBTAINING A
PLANT EXTRACT**(30) **Foreign Application Priority Data**Mar. 28, 2000 (DE)..... 100 15 353.4
Nov. 16, 2000 (DE)..... 100 56 902.1**Publication Classification**(76) **Inventor: Armin Scheffler, Niefern-Oschelbronn
(DE)**(51) **Int. Cl.⁷ C11D 17/00**(52) **U.S. Cl. 510/417****Correspondence Address:**
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PO Box 20445
Tampa, FL 33622-0445 (US)(57) **ABSTRACT**

The relates to a method for obtaining triterpenes from plants and/or the constituents thereof, in addition to an emulsion whose aqueous and fatty phase is emulsified by the plant extract. The plant extract contains at least one triterpene and/or a triterpene derivative and the emulsion contains at least one oil and/or fat and water. The invention further relates to a method for production of said emulsion and to the use of said triterpenes in the production of cosmetics and medicaments.

(21) **Appl. No.: 10/239,929**(22) **PCT Filed: Mar. 26, 2001**(86) **PCT No.: PCT/EP01/03417**

**EMULSION CONTAINING A PLANT EXTRACT,
METHOD FOR PRODUCING SAID EMULSION
AND FOR OBTAINING A PLANT EXTRACT**

[0001] The present invention concerns a process for obtaining triterpenes and/or their components as well as an emulsion, of which the aqueous and fatty phases are emulsified by a plant extract, wherein the plant extract contains at least one triterpene and/or a triterpene derivative and the emulsion further contains at least one oil and/or fat and water. Besides this, the present invention concerns a process for producing the emulsion as well as the use of the triterpenes for production of cosmetics and pharmaceuticals.

[0002] Natural ingredients, fragrances or flavors and active substances have for a long time been isolated, using various extraction techniques, from whole plants and their parts, such as leaves, roots, fruits or bark. As one of the first natural substances, betulin (birch camphor), the substance which imparts to birch bark its white color, was extracted from plant material in the year 1788 (Lowitz, M., *Chemische Analysen*, Hrsg. Crell, L., Vol. 2, page 312). Subsequent to this first isolation there followed scientific studies, including elementary analysis of betulin, which were published by U. Hausmann 1876 (Hausmann, U., *Annalen der Chemis*, 182, page 368).

[0003] Betulin containing plants are widely distributed in the plant kingdom. They belong primarily to the Hamamelidaceae (angiosperm plants), where in one single species in the order fagales (birch relatives), and more particularly in the family of the betulaceae (birches), the content of betulin accumulates in the outer bark (review article: Hayek, E. W. et al., (1989), *A Bicentennial of Betulin*, *Phytochemistry*, 28(9), pages 2229-2242). The white part of the birch bark, in particular the species *betula pedula*, *betula verrucosa* and *betula papyfera* can contain more than 30% betulin. More precise research was published by Rainer Ekman in the year 1983, according to which 21-40% triterpene, or 16.7-34% betulin, were extracted from the dry outer bark of *betula verrucosa* (Ekman, R. (1983a), *Holzforschung*, 37, page 205-211). The inner bark, in comparison, contained only traces of triterpenes, in the realm of approximately 0.37-0.43% (Ekman, R. (1983b), *Finn. Chem. Letters*, page 162).

[0004] Betulin is a pentacyclic triterpene with a lupan skeleton, which is also referred to as betulolol, trochoton, birch camphor and (coryli) resinol. The characterizing feature of the lupan group is a ring with five carbon atoms within the pentacyclic system, which contains an α -isopentenyl group in the position C-19. Betulin is further characterized by a high thermal stability, its melting point lies between 250 and 260° C., wherein even high values are obtained after sublimation of the re-crystallized product. Its molecular weight is 442.7, it is soluble in pyridine and tetrahydrofuran, however only slightly soluble in dichloromethane, chloroform and cold organic solvents, wherein its solubility however significantly increases with increasing temperature. In water and cold petroleum ether [carbohydrate with 5 to 8 C-atoms (C_5-C_8 CH)] betulin is practically insoluble. Besides this, kinetic research has shown low reactivity of the hydroxy group of betulin (review article: Jääskeläinen, P. (1981), *Paperi ja Puu—Papper och Trä* 10, pages 599-603).

[0005] Already in the year 1899 J. Wheeler demonstrated the antiseptic characteristics of betulin, it is thus used for

sterilization of bandages and adhesive medical plaster (Wheeler, J. 1899), *Pharm. J.*, The Production of Betulin by Sublimation, 494, *Ref. Chem. Centr.* 1900 I, page 353). In natural medicine and folk remedies products from cooking birch bark were and are still employed, wherein however only the inner part is used, which contains only residue of the white birch bark and, due to its low solubility, most likely contains no betulin, since the content of betulin in the inner bark is less than 0.5% and betulin is insoluble in water or water-alcohol mixtures (up to 60% alcohol) (Ekman, R. (1983b), *supra*).

[0006] The thus obtained product of boiling is used for treatment of hot flashes, water craving, gout and for skin diseases, as well as a tincture for bandages for abscesses. Further, birch bark is used for production of birch bark oil, which has also been used for treatment of rheumatism and as aroma therapy (Hansel, R. et al., (Hrsg.), (1994), *Drug A-D*, Springer Publishing House, Chapter *Betula*, pages 502-511; Hyek, E. W. *supra*). Besides this, the use of birch extracts as bath salts for treatment, particularly for sweaty feet, as well as additives to shampoos as a hair care agent is known (Nowak, G. A., (1966), *Cosmetic and Medicinal Properties of the Birch*, *Amer. Perfumer Cosmet.*, 81, page 37). Here, however, only aqueous extracts from birch leaves have been employed, which contain practically no betulin.

[0007] Newer research suggests a medicinal effect of betulin and betulin derivatives. In animal tests betulonic acid inhibited the replication of retroviruses, in particular the human immune deficiency virus (HIV1). The published bacteriostatic and bactericidal effect of betulin against intestinal *Escherichia coli*, *Salmonella typhi*, *Shigella flexneri* and *Staphylococcus aureus* suggest a broader medicinal application (Chen Sun, J. et al., (1998), *Anti-AIDS Agents*, 32, *Synthesis and anti-HIV activity of Betulin derivatives*, *Bioorganic & Medical Chemistry Letters* 8, pages 1267-1272; Evers, M. et al., (1996), *Betulonic acid derivatives: a new class of human immunodeficiency virus type 1 specific inhibitors with a new mode of action*, *J. Med. Chem.* 39, pages 1056-1068; Hayek, E. W. et al., *supra*). Further an anti-inflammatory, cortisone like effect as well as cytostatic effect upon use in vitro against various tumor cell lines of betulin and betulin derivatives has been shown (Carmen Recio, M., et al. (1995), *Investigations on the steroidal anti-inflammatory activity of triterpenoids from Diospyros leucomelas*, *Planta Med.* 61, pages 9-12; Yasukawa, K., et al., (1991), *Sterol and triterpene derivatives from plants* (...), *Oncogene* 48, pages 72-76).

[0008] For obtaining betulin from birch bark, in particular from birch cork, one could consider using, besides sublimation (Lowitz, M., *supra*), above all extraction in boiling solvents. As solvent there are employed mainly alcohol and chlorinated carbohydrates (Ukkonen, K. and Era, V., (1979), *Kemia-Kemi* 5, pages 217-220; Ekman, R. (1983a), *supra*; Eckermann, C. and Ekman, R., (1985), *Paperi ja Puu—Papper och Trä* 3, pages 100-106; O'Connell, M. M. et al., (1988), *Phytochemistry* 7, pages 2175-2176; Hua, Y. et al., (1991), *Journal of Wood Chemistry and Technology* 11(4), pages 503-516).

[0009] The disadvantage of the sublimation technique is the fact that the content is obtained only with very low yield, which necessitates the use of large amounts of starting materials. Besides this, a particular disadvantage of the

would have had a negative influence on the degree of purity following extraction. In order to further increase the degree of purity, the extracted components can be subsequently post washed with fresh solvent.

[0034] In a preferred embodiment the first washing step is carried under a pressure of 1 to 300 bar, preferably 10 to 35 bar, particularly preferably about 25 bar. The actual extraction occurs preferably at a temperature of 50 to 200° C., preferably 140 to 160° C., particularly preferably about 150° C. and under a pressure of 1 to 300 bar, preferably 10 to 35 bar, particularly preferably about 25 bar. In these extraction conditions large amounts of pure triterpenes, in particular pure betulin, are obtained.

[0035] The inventive process has also been found to be of particular advantage, when the crystallization of the triterpene occurs as micro-crystallization with an average particle size of <40 µm, in particular from 2 to 32 µm.

[0036] A further attribute of the present invention is an emulsion, of which the aqueous and fatty phases are emulsified by a plant extract, wherein the plant extract includes at least one triterpene and/or at least one derivative of a triterpene and the emulsion further includes at least one oil and/or fat and water.

[0037] The triterpene and/or its derivative preserves and emulsifies the emulsion. Besides this, it is pharmaceutically active. Thereby it is in particular achieved, that the emulsion contains no supplemental preservative, and thus possesses a particularly high degree of purity and a good compatibility above all with problematic applications to damaged skin.

[0038] The plant extract is herein an extract of birch bark, preferably from the white part of the birch bark, which is referred to as birch cork.

[0039] In a further embodiment the plant extract contains at least one of the substances betulin, betulinic acid, betulonic acid, lupeol (lupol), erythrodil, allobetulin, phellonic acid, hydroxy-lactone, betulonic aldehyde, β-amyrin, oleanolic acid, ursolic acid, esterified betulin and/or β-sitosterol. These plant constituents could be employed individually as well as mixed with each other in various combinations in the inventive emulsion. A particularly suitable combination is comprised of betulin >80%, betulinic acid <10%, lupeol <3%, oleanolic acid <4%, erythrodil <4% and water <1%.

[0040] The emulsion preferably contains the triterpene and/or its derivative in a concentration of 2 to 10%. Depending upon the desired consistency, the proportion of the triterpene and/or its derivative can be varied in the mentioned concentration range. For the employment of a fluid lotion the emulsion exhibits for example a concentration of the triterpene and/or its derivative of 2 to 3.5%. If the emulsion is used in the form of a cream, the concentration of the triterpene and/or its derivative is preferably 3.5 and 10%.

[0041] The oily and/or fatty component of the emulsion can be selected from any of the dermatological and cosmetic known oils and fats. Particularly suitable are animal and plant fats such as jojoba oil, peanut oil and olive oil. Particularly preferred is the use of avocado and/or almond oil.

[0042] In order to regulate the consistency of the inventive emulsion, conventional moisturizers and/or thickeners and

solidifiers can be employed. As moisturizers there can be employed in particular glycerin and urea or carbamide. Herein above all concentrations of respectively 3 to 10% glycerin and/or urea or carbamide are suitable based upon the amount of the emulsion. As thickener there can be employed, for example, polysaccharides, which are to be added in a concentration of 0.2 to 2%, preferably 0.5%, based upon the amount of the employed water. Natural polysaccharides as well as further sugar compounds and their derivatives are particularly suitable, since they do not react with the other components of the emulsion, they do not modify them and are thus chemically inert.

[0043] Thus the polysaccharide agar agar is preferably employed. Agar agar is a mixture of agarose and agarpectin, which is obtained from red algae and has the advantage that it cannot be decomposed by most micro-organisms. Alternatively, the polysaccharide carrageenan can be employed which occurs naturally in the cell wall of red algae and certain brown algae and has the same advantages as agar agar.

[0044] In a further embodiment the emulsion comprises 2 to 10% extract from the white part of the birch bark, 20 to 30% avocado oil, 10 to 20% almond oil and 40 to 68% water. The most preferred concentrations comprise 4% extract from the white part of the birch bark, 29.3% avocado oil, 14.7% almond oil and 52% water.

[0045] A further inventive emulsion contains 2 to 10% extract from the white part of the birch bark, 20 to 30% avocado oil, 10 to 20% almond oil, 5 to 10% moisturizing agent and 30 to 63% water. Herein the most preferred is the concentration of 4% extract from the white part of the birch bark, 29.3% avocado oil, 14.7% almond oil, 5% glycerin and/or 5% urea and 42 to 47% water.

[0046] The extract from the white part of the birch bark, which is contained in all emulsions, comprises at least 80% betulin, at most 10% betulinic acid, at most 3% lupeol and at most 4% oleanolic acid.

[0047] The emulsion, on the basis of its composition and its verifiable biocompatibility, is particularly suitable as a salve base for addition of all known fragrances, cosmetics and medicinal active agents.

[0048] A further attribute of the invention is a process for producing the inventive emulsion, wherein the process includes the following steps:

[0049] (a) dispersion of triterpene in an oil and/or fat;

[0050] (b) emulsification of water;

[0051] (c) homogenization of the emulsion to the desired consistency.

[0052] Herein the dispersion and homogenization preferably occurs in a homogenizing mixer since the process can be carried in particularly simple manner in this way. Further, it is possible to prepare small amounts of emulsion for individual applications.

[0053] In a particularly preferred embodiment there is added to the water which is used during emulsification a moisturizing agent, in particular glycerin and/or urea, or a thickener, in particular a polysaccharide. Thereby a particularly creamy consistency can be achieved.

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solidic es este prod. intermediario

[0054] A further attribute of the present invention is the use of the triterpenes for manufacture of a cosmetic, preferably in the form of a salve, a lotion, a cream, a gel, a jelly, a tincture, a shampoo, a powder and/or a cosmetic (compact) powder, in particular for application upon the skin, the face or scalp or scalp and/or for inhalation. On the basis of its chemical relationship to sterols the triterpenes, in particular the obtained betulin, are particularly suitable for skin and head care. It relaxes and smoothes skin, reduces the water loss and induces attractiveness and blush. Thereby the cosmetic can be particularly employed for maintaining moisture of the skin and smoothing the skin as well as for reduction of age spots and can be employed in the case of dandruff or flaking skin. A further advantage is the water insolubility of the triterpenes, so that skin which is exposed to water vigorously and for prolonged periods is particularly well protected. On the basis of the anti-bacterial effect the use as deodorant is particularly advantageous. Added to this is the minimization of transpiration on the basis of an effective closure of the sweat glands.

[0055] A further attribute of the present invention is the use of the triterpenes for production of a pharmaceutical or medicinal formulation, preferably in the form of a salve, a lotion, a cream, a gel, a jelly, a tincture, a shampoo, a powder and/or a cosmetic (compact) powder, in particular for application upon the skin, the face or scalp or scalp, and/or for inhalation, particularly preferably for treatment of dermatological conditions of the skin and/or the scalp, above all for neurodermitis, psoriasis, contact eczema, melanoderma, impetigo, pre-cancerous conditions of the skin as well as for inhalation during asthmatic attacks and/or for substitution in place of glucocorticoids. Likewise, on the basis of their high purity, the obtained triterpenes, in particular the obtained betulin, is suitable for the therapeutic application on pre-cancerous skin.

[0056] The inventive emulsion is so well suited for the above-mentioned applications because the extract from the white part of the birch bark includes no mutagenic characteristics. Topical toxicity tests were likewise carried out, wherefrom no sensitizing characteristics were discovered.

[0057] The following examples serve for illustrating and imparting a better understanding of the present invention, but should in no way be considered as limitations.

EXAMPLES

I. Clinical Observations

[0058] Various clinic observations of dermatological skin changes were carried out by general practice doctors as well as clinical doctors. Following the diagnosis by the doctors there occurred a treatment of the patients with the inventive emulsion, which was produced in accordance with described processes.

Example 1

[0059] Patient: male, 68 years

[0060] Diagnosis: heavy, generalized psoriasis vulgaris

[0061] Pre-Treatment: medium strength cortisone salve

[0062] Application: scalp

[0063] Treatment: multiple daily application of the inventive emulsion as salve upon the afflicted skin areas

[0064] Results: the occurrence of psoriasis efflorescence following application of the cortisone salve was prevented by the application of the inventive emulsion

Example 2

[0065] Patient: male, 48 years

[0066] Diagnosis: light psoriasis vulgaris

[0067] Pre-Treatment: medium strength cortisone salve

[0068] Application: head

[0069] Treatment: multiple daily application of the inventive emulsion as salve upon the afflicted skin areas

[0070] Results: healing of the approximately dollar-piece sized presternal inflamed focal areas of the infection on the head upon application of the inventive emulsion within 14 days; re-inflammation of the infection (=recidivist) after cessation of application of emulsion; renewed definite improvement upon resumption of the treatment

Example 3

[0071] Patient: female, 5 months

[0072] Diagnosis: neurodermitis, hyperkeratotic, prematurely aged, chapped-shriveled skin

[0073] Application: body

[0074] Treatment: multiple daily applications of the inventive emulsion as salve upon the afflicted skin areas

[0075] Results: very noticeable improvement, excellent effectiveness with simultaneously good compatibility

Example 4

[0076] Patient: female, 10 years

[0077] Diagnosis: neurodermitis, hyperkeratotic, prematurely aged, chapped-shriveled skin

[0078] Application: body

[0079] Treatment: multiple daily applications of the inventive emulsion as salve upon the afflicted skin areas

[0080] Results: very noticeable improvement, excellent effectiveness with simultaneously good compatibility

Example 5

[0081] Patient: male, 5 months

[0082] Diagnosis: neurodermitis, hyperkeratotic, prematurely aged, chapped-shriveled skin

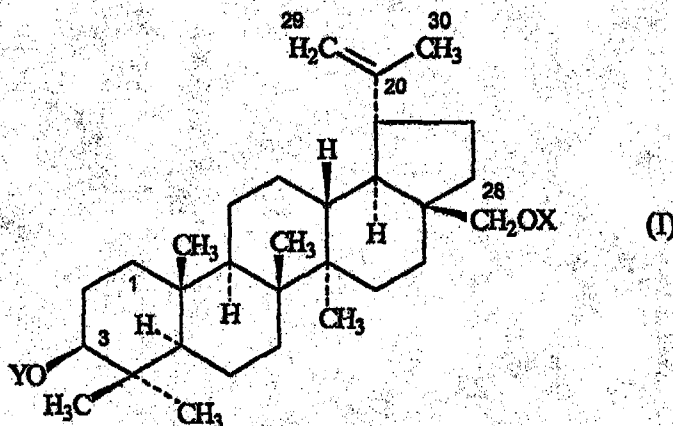
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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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(21) International Application Number: PCT/US98/02445 (22) International Filing Date: 11 February 1998 (11.02.98) (30) Priority Data: 08/798,900 11 February 1997 (11.02.97) US (63) Related by Continuation (CON) or Continuation-in-Part (CIP) to Earlier Application US 08/798,900 (CIP) Filed on 11 February 1997 (11.02.97) (71) Applicant (for all designated States except US): REGENTS OF THE UNIVERSITY OF MINNESOTA [US/US]; Morrill Hall, 100 Church Street S.E., Minneapolis, MN 55455 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): CARLSON, Robert, M. [US/US]; 2231 East Third Street, Duluth, MN 55812 (US). KRASUTSKY, Pavel, A. [UA/US]; 6004 London Road, Duluth, MN 55804 (US). KARIM, M., Reza-UI [US/US]; 2323 East First Street, Duluth, MN 55812 (US). (74) Agent: VIKSNINS, Ann, S.; Schwegman, Lundberg, Woessner & Kluth, P.O. Box 2938, Minneapolis, MN 55402 (US).	(81) Designated States: CA, JP, US, European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE). Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>	
(54) Title: USE OF BETULIN AND ANALOGS THEREOF TO TREAT HERPESVIRUS INFECTION (57) Abstract A therapeutic method is provided for treating a mammal afflicted with a herpesvirus infection, comprising administering an effective amount of betulin or a derivative thereof. The invention also provides novel betulin derivatives, pharmaceutical compositions comprising novel betulin derivatives, novel betulin derivatives for use in medical therapy, and the use of betulin derivatives to prepare a medicament useful for treating herpesvirus infection.		

There is an increasing need for antiviral and antibacterial agents, because of therapeutic complications due to the emergence of new bacteria and viruses, and mutations of the old viral and bacterial species.

The present invention provides a therapeutic method for the treatment of herpesvirus infection comprising administering to a mammal, such as a human, afflicted with a herpesvirus infection, an effective anti-viral amount of a compound of formula (I):



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Compounds of formula I wherein X is (C₁-C₆)alkanoyl can be prepared from a corresponding compound wherein X is H by reaction with the requisite (C₁-C₆)alkanoyl-Cl.

Compounds of formula I wherein Y is (C₁-C₆)alkanoyl can be prepared from a corresponding compound wherein Y is H by reaction with the requisite (C₁-C₆)alkanoyl-Cl.

The compound of formula I dichlorooxalylbetulin is also a useful intermediate for preparing other compounds of formula I wherein X and Y are -C(=O)C(=O)R_k.

The compound of formula I 28-chlorooxalylbetulin is also a useful intermediate for preparing other compounds of formula I wherein X is -C(=O)C(=O)R_k.

Pharmaceutically acceptable salts include nontoxic amine salts and alkali metal salts of phosphates and nontoxic inorganic and organic acid addition salts of amines, such as the citrate, malonate, malate, tartarate, hydrochloride, sulfate, bicarbonate, and carbonate salts.

The compounds of formula (I) can be formulated as pharmaceutical compositions and administered to a mammalian host, such as a human patient afflicted with herpesvirus infection, in a variety of forms adapted to the chosen route of administration, i.e., orally or parenterally, by intravenous, intramuscular, topical or subcutaneous routes.

Thus, the present compounds may be systemically administered, e.g., orally, in combination with a pharmaceutically acceptable vehicle such as an inert diluent or an assimilable edible carrier. They may be enclosed in hard or soft shell gelatin capsules, may be compressed into tablets, or may be incorporated directly with the food of the patient's diet. For oral therapeutic administration, the active compound may be combined with one or more excipients and used in the form of ingestible tablets, buccal tablets, troches, capsules, elixirs, suspensions, syrups, wafers, and the like. Such compositions and preparations should contain at least 0.1% of active compound. The percentage of the compositions and preparations may, of course, be varied and

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may conveniently be between about 2 to about 60% of the weight of a given unit dosage form. The amount of active compound in such therapeutically useful compositions is such that an effective dosage level will be obtained.

The tablets, troches, pills, capsules, and the like may also contain

5 the following: binders such as gum tragacanth, acacia, corn starch or gelatin; excipients such as dicalcium phosphate; a disintegrating agent such as corn starch, potato starch, alginic acid and the like; a lubricant such as magnesium stearate; and a sweetening agent such as sucrose, fructose, lactose or aspartame or a flavoring agent such as peppermint, oil of wintergreen, or cherry flavoring

10 may be added. When the unit dosage form is a capsule, it may contain, in addition to materials of the above type, a liquid carrier, such as a vegetable oil or a polyethylene glycol. Various other materials may be present as coatings or to otherwise modify the physical form of the solid unit dosage form. For instance, tablets, pills, or capsules may be coated with gelatin, wax, shellac or sugar and

15 the like. A syrup or elixir may contain the active compound, sucrose or fructose as a sweetening agent, methyl and propylparabens as preservatives, a dye and flavoring such as cherry or orange flavor. Of course, any material used in preparing any unit dosage form should be pharmaceutically acceptable and substantially non-toxic in the amounts employed. In addition, the active

20 compound may be incorporated into sustained-release preparations and devices.

The active compound may also be administered intravenously or intraperitoneally by infusion or injection. Solutions of the active compound or its salts can be prepared in water, optionally mixed with a nontoxic surfactant. Dispersions can also be prepared in glycerol, liquid polyethylene glycols,

25 triacetin, and mixtures thereof and in oils. Under ordinary conditions of storage and use, these preparations contain a preservative to prevent the growth of microorganisms.

The pharmaceutical dosage forms suitable for injection or infusion can include sterile aqueous solutions or dispersions or sterile powders

30 comprising the active ingredient which are adapted for the extemporaneous preparation of sterile injectable or infusable solutions or dispersions, optionally

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and additional antimicrobial agents can be added to optimize the properties for a given use. The resultant liquid compositions can be applied from absorbent pads, used to impregnate bandages and other dressings, or sprayed onto the affected area using pump-type or aerosol sprayers. The liquid compositions can also be employed as eyedrops, mouth washes, douches, etc. Antibacterial presaturated wipes are disclosed by Anderson (U.S. Pat. No. 4,896,768).

Thickeners such as synthetic polymers, fatty acids, fatty acid salts and esters, fatty alcohols, modified celluloses or modified mineral materials can also be employed with liquid carriers to form spreadable pastes, gels, ointments, soaps, and the like, for application directly to the skin of the user.

Other examples of useful dermatological compositions which can be used to deliver the compounds of formula (I) to the skin are disclosed in Jacquet et al. (U.S. Pat. No. 4,608,392), Geria (U.S. Pat. No. 4,992,478), Smith et al. (U.S. Pat. No. 4,559,157) and Wortzman (U.S. Pat. No. 4,820,508).

Useful dosages of the compounds of formula (I) can be determined by comparing their *in vitro* activity, and *in vivo* activity in animal models. Methods for the extrapolation of effective dosages in mice, and other animals, to humans are known to the art; for example, see U.S. Pat. No. 4,938,949.

Generally, the concentration of the compound(s) of formula (I) in a liquid composition, such as a lotion, will be from about 0.1-25 wt-%, preferably from about 0.5-10 wt-%. The concentration in a semi-solid or solid composition such as a gel or a powder will be about 0.1-5 wt-%, preferably about 0.5-2.5 wt-%. Single dosages for injection, infusion or ingestion will generally vary between 50-1500 mg, and may be administered, i.e., 1-3 times daily, to yield levels of about 0.5 - 50 mg/kg, for adults.

The invention will be further described by reference to the following detailed examples.

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EXAMPLE 1

Betulin extraction and purification



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Bhaggan et al.

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(54) **FAT BLENDS WITH CRYSTAL MODIFIERS**

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(57) **ABSTRACT**

Blends containing a vegetable fat or a blend of vegetable fats and at least 0.1 wt % of a composition comprising ursolic acid and oleanolic acid in a weight ratio of 1:99 to 99:1 display a number of benefits such as high crystallisation rates. This modification of the crystallisation rate can be used to achieve a number of beneficial effects in the final fat blend or in the final food product containing the blend.

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[0078] Dimension at 40° C.:

Ref	4.0 × 4.3 cm	Height	0.8-1.0 cm
M1	4.0 × 3.8 cm	Height	1.0-1.2 cm
M2	3.3 × 3.0 cm	Height	1.5-1.7 cm

[0079] The highest heat resistance was observed with ursolic acid extract containing sample.

[0080] Hardness

[0081] The settings on the Stevens Texture Analyzer were:

[0082] Distance: 2 mm

[0083] Speed: 0.5 mm/sec.

	Ref	M1	M2
<u>Temperature 20° C.</u>			
1 day	195	188	201
1 week	195	184	206
1 month	200	186	219
2 months	198	188	232
2 months	203	184	224
<u>Temperature 25° C.</u>			
1 day	129	130	144
1 week	167	165	164
1 month	158	168	174
<u>Temperature 30° C.</u>			
1 day	58	65	60
1 week	53	62	61
1 month	146	127	165

[0084] The chocolate with ursolic acid extract were found to have better hardness at all temperatures between 1 to 3 month of storage.

[0085] 5. Effects of ursolic acid extract on aeration properties

[0086] Experimental

[0087] The coatings were aerated for 20 minutes by using the Hobart N-50.

[0088] The samples were measured for density and hardness.

[0089] Coating A: 475 gram Callebaut 811±10 gram P060+15 gram CCB

[0090] Coating B: 475 gram Callebaut 811±10 gram Ursolic acid+15 gram CCB

[0091] Results

[0092] Density measurement:

[0093] The coating was weighed in a metal cup with a known volume of 90 cm³. A summary of the data is given in the table below. The density can then be calculated with the formula:

$$\text{Density} = \frac{\text{mass(gram)}}{\text{volume(cm}^3\text{)}}$$

[0094] Hardness measurement:

[0095] The aerated coating was kept at 20° C. for 2 days before measurement. The settings on the Stevens Texture Analyzer were:

[0096] Distance: 2 mm

[0097] Speed: 0.5 mm/sec.

[0098] A summary of the hardness (load in grams) is given in the table as well.

[0099] Results

	Coating A	Coating B	Units
Mass before aerating	111.5	110.3	gram
Density before aerating	1.24	1.23	g/cm ³
Mass after aerating	106.1	105	gram
Density after aerating	1.18	1.17	g/cm ³
Air	4.8	4.8	%
Hardness	188	199	gram

[0100] Conclusion

[0101] In both coatings the same amount of air was determined after aeration whereas the hardness of the aerated coating with ursolic acid extract was found to be higher.

1. Blend of a vegetable fat and/or a blend of vegetable fats and at least 0.1 wt %, preferably 0.1 to 10 wt %, most preferably 0.2 to 5 wt % of a natural health composition, wherein the natural health composition comprises a mixture of ursolic acid and oleanolic acid in a weight ratio of 1:99 to 99:1, preferably 10:90 to 90:10, more preferably 75:25 to 25:75.

2. Blend according to claim 1 wherein the fat displays a solid fat content measured on a non-stabilised fat by NMR-pulse at the temperature indicated of: 5 to 90 at 5° C.; 2 to 80 at 20° C. and less than 15 at 35° C.

3. Blend according to claim 1 wherein the blend comprises components A, B and C, wherein

A=a natural health composition comprising a mixture of ursolic acid and oleanolic acid in a weight ratio of 1:99 to 99:1

B=a solid fat with a solid fat content at 20° C. of at least 20, measured on the unstabilised fat by NMR-pulse, preferably at least 45, most preferably at least 60 and

C=a fat with a content of fatty acids with 18 C-atoms with one to three double bonds of at least 40%,

which components a, b and c are present in amounts of:

at least 0.1 wt % A, preferably 0.1 to 20 wt %, most preferably 0.2 to 10 wt %

8 to 90 wt % of B, preferably 25 to 75 wt %, most preferably 40 to 70 wt % and

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0 to 85 wt % of C, preferably 15 to 65 wt %, most preferably 20 to 50 wt %.

4. Blend according to claim 3 wherein fat B is selected from the group consisting of palm oil, palm oil fractions, cocoa butter, cocoa butter equivalents, palm kernel oil, fractions of palm kernel oil, hardened vegetable oils such as hardened palm oil, hardened fractions of palm oil, hardened soybean oil, hardened sunflower oil, hardened rape seed oil, hardened fractions of soy, rape or sunflower oil, mixtures of one or more of these oils and interesterified mixtures thereof.

5. Blend according to claim 3 wherein fat C is selected from the group consisting of sunflower oil, high oleic sunflower oil, olive oil, soybean oil, rape seed oil, palm oil olein, olein fractions from vegetable oils, high oleic vegetable oils and cotton seed oil.

6. Blend according to claim 1 wherein the natural health composition also comprises isoflavonoids and/or flavonoids in amounts corresponding with 0.005 to 5% of the total amount of ursolic acid and oleanolic acid.

7. Blend according to claim 1, wherein the natural health composition is obtained from fruit skins, in particular from the skins of apples, pears, cranberries, cherries or prunes.

8. Food products with a fat phase wherein the fat phase comprises at least partly the blend according to any of claims 1 to 7.

9. Food products according to claim 8, wherein the food product is selected from the group consisting of spreads (low fat or full fat), dressings, mayonnaises, cheese, creams, ice creams, ice cream coatings, confectionery coatings, fillings, sauces and culinary products

10. Food products according to claim 9, wherein the food product comprises 10 to 90 wt %, preferably 20 to 60 wt % of a continuous fat phase.

11. Method to modify the crystallisation behavior of a fat blend or a fat blend in a final food product to

(i) increase the hardness of the fat blend or final product and/or

(ii) to improve the plasticity of the fat blend or final product and/or

(iii) to improve oral mouthfeel of the fat blend or final product and/or

(iv) to improve the heat resistance of the fat blend or final product and/or

(v) to increase the speed of crystallisation of the fat blend or final product and/or

(vi) to increase the aeration properties of the fat blend or final product and/or

(vii) to decrease drying times of ice-cream coatings, by incorporating an effective amount of a blend of ursolic acid and oleanolic acid in the fat blend per se or in a fat blend of a food product

12. Process to make a blend with the composition according to any of 1 to 7 claims, wherein

(i) skins of a fruit such as apples, cherries, prunes and pears are extracted with an organic solvent such as acetone

(ii) an extract of a mixture of ursolic acid and oleanolic acid is isolated and after removal of the solvent a mixture containing ursolic acid and oleanolic acid is obtained

(iii) this mixture of acids obtained in (ii) is blended with a fat in the ratios required to obtain the compositions according to claims 1 to 7.

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(54) Title: COMPOSITION CONTAINING EXTRACTS OF BUTYROSPERMUM PARKII AND THE USE AS MEDICAMENT OR DIETARY SUPPLEMENT

(57) Abstract: The present invention relates to a composition comprising an extract or a concentrate of *Butyrospermum parkii* as a dietary supplement or a pharmaceutical composition and to the use of such compositions for the preparation of a medicament or a dietary supplement for the suppression of hypersensitivity and/or inflammatory reaction. The composition may optionally be formulated with a pharmaceutically acceptable carrier for systemic or topical administration. More specifically, the invention relates to a dietary supplement or a pharmaceutical composition comprising an extract or a concentrate of *Butyrospermum parkii*, wherein said extract

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COMPOSITION CONTAINING EXTRACTS OF BUTYROSPERMUM PARKII AND THE USE AS MEDICAMENT OR DIETARY SUPPLEMENT

5 FIELD OF THE INVENTION

The present invention relates to a dietary supplement or a pharmaceutical composition for systemic or topical administration comprising an extract or a concentrate of *Butyrospermum parkii* optionally formulated with a pharmaceutically acceptable carrier for systemic or topical administration. More specifically, the invention relates to a dietary

10 supplement or a pharmaceutical composition comprising an extract or a concentrate of *Butyrospermum parkii*, wherein said extract or concentrate contains the triterpene alcohols butyrospermol, lupeol, parkeol, germanicol, dammaradienol, 24-methylene-dammarenol, α -amyirin and β -amyirin and optionally the sterols stigmasterol, avanasterol, 24-methyl-cholest-7-enol, karitesterol A, karitesterol B and α -spinasterol, and to the use of

15 such compositions for the preparation of a medicament or a dietary supplement for the suppression of hypersensitivity and/or inflammatory reaction.

BACKGROUND OF THE INVENTION

Hypersensitivity is defined as a state of altered reactivity in which the body reacts with an

20 exaggerated immune response to a substance (antigen). Hypersensitivity may be caused by exogenous or endogenous antigens.

Hypersensitivity reactions underlie a large number of diseases. Among these, allergic and autoimmune conditions are of great importance. A classification of hypersensitivity dis-

25 eases is given in the textbook Clinical Medicine (Kumar, P. and Clark, M.: "Clinical Medicine", 3rd edition, p. 147-150, 1994, Bailliere Tindall, London).

Type I hypersensitivity reactions (IgE mediated allergic reactions) are caused by allergens (specific exogenous antigens), e.g. pollen, house dust, animal dandruff, moulds, etc. Aller-

30 gic diseases in which type I reactions play a significant role include asthma, eczema (atopic dermatitis), urticaria, allergic rhinitis and anaphylaxis.

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for the treatment or prevention of an autoimmune disorder in a mammal, said method comprising administering said composition to said mammal; and the invention comprises the use of said composition for the preparation of a medicament for the treatment or prevention of autoimmune disorders in a mammal.

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Further, according to the invention a composition comprising an extract or a concentrate of *Butyrospermum parkii* as described above for systemic administration and optionally a pharmaceutically acceptable carrier for systemic administration can be used in a method for the treatment or prevention of an IgE mediated allergic reaction or condition in a

10 mammal, said method comprising administering said composition to said mammal; and the invention comprises the use of said composition for the preparation of a medicament for the treatment or prevention of IgE mediated allergic reactions and conditions in a mammal.

15 Also, according to the invention a composition comprising an extract or a concentrate of *Butyrospermum parkii* as described above for systemic administration and optionally a pharmaceutically acceptable carrier for systemic administration can be used in a method for the alleviation of pain in a mammal, said method comprising administering said composition to said mammal; and the invention comprises the use of said composition for the
20 preparation of a medicament for the alleviation of pain in a mammal.

Also, the present invention provides a pharmaceutical composition, comprising: i) at least 5% (w/w) Butyrospermum-triterpenes; ii) an extract of *Calendula officinalis*; and optionally
25 ii) a pharmaceutically acceptable carrier. Preferably, for topical administration to the skin or mucous membranes.

Thus, the present invention provides a pharmaceutical composition containing at least 5% Butyrospermum-triterpenes, wherein the pharmaceutical composition is formulated as a fluid, ointment, gel, liniment, emulsion (e.g. cream or lotion) or spray (e.g. aerosol).

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According to the invention a pharmaceutical composition comprising at least 5% Butyrospermum-triterpenes and optionally a pharmaceutically acceptable carrier can be used in a method for the treatment or prevention of inflammation or hypersensitivity of the skin or mucous membranes in a mammal, said method comprising administering said composition
35 topically to said mammal; and the invention comprises the use of said composition

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5 vant to all known diseases associated with hypersensitivity reactions or inflammation, including autoimmune disorders and IgE mediated allergic conditions. The action of the above mentioned pharmaceutical compositions according to the invention is relevant to all known conditions and diseases associated with hypersensitivity reaction, and the following examples are not limiting with respect to this: infections (viral, bacterial, fungal, parasitic, etc.), cold and flu, contact dermatitis, insect bites, allergic vasculitis, postoperative reactions, transplantation rejection (graft-versus-host disease), asthma, eczema (e.g. atopic dermatitis), urticaria, allergic rhinitis, anaphylaxis, autoimmune hepatitis, Primary biliary cirrhosis, Primary sclerosing cholangitis, Autoimmune hemolytic anemias, Grave's
10 disease, Myasthenia gravis, Type 1 Diabetes Mellitus, Inflammatory myopathies, Multiple sclerosis, Hashimoto's thyroiditis, Autoimmune adrenalitis, Crohn's Disease, Ulcerative Colitis, Glomerulonephritis, Progressive Systemic Sclerosis (Scleroderma), Sjögren's Disease, Lupus Erythematosus, Primary vasculitis, Rheumatoid Arthritis, Juvenile Arthritis, Mixed Connective Tissue Disease, Psoriasis, Pemfigus, Pemfigoid, Dermatitis Herpeti-
15 formis, etc.

According to the invention the above mentioned compositions can be combined with any other active ingredient(s) to potentiate the therapeutic action.

20 A pharmaceutical acceptable carrier for systemic or topical administration can be water or vehicles other than water, said other vehicles can be used in the compositions and can include solids or liquids such as solvents, thickeners and powders. Examples of each of these types of vehicles, which can be used singly or as compositions of one or more vehicles, are as follows:

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Emollients, such as stearyl alcohol, glyceryl monoricinoleate, glyceryl monostearate, propane-1,2-diol, butane-1,3-diol, cetyl alcohol, isopropyl isostearate, stearic acid, isobutyl palmitate, isocetyl stearate, oleyl alcohol, isopropyl laurate, hexyl laurate, decyl oleate, octadecan-2-ol, isocetyl alcohol, cetyl palmitate, dimethylpolysiloxane, di-n-butyl seba-
30 cate, isopropyl myristate, isopropyl palmitate, isopropyl stearate, butyl stearate, polyethylene glycol, triethylene glycol, lanolin, castor oil, acetylated lanolin alcohols, petroleum, mineral oil, butyl myristate, isostearic acid, palmitic acid, isopropyl linoleate, lauryl lactate, myristyl lactate, decyl oleate, myristyl myristate;

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solvents, such as water, methylene chloride, isopropanol, castor oil, ethylene glycol monoethyl ether, diethylene glycol monobutyl ether, diethylene glycol monoethyl ether, dimethyl sulfoxide, tetrahydrofuran, vegetable and animal oils, glycerol, ethanol, propanol, propylene glycol, and other glycols or alcohols, fixed oils;

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humectants or moistening agents, such as glycerin, sorbitol, sodium 2-pyrrolidone-5-carboxylate, soluble collagen, dibutyl phthalate, gelatin;

10 powders, such as chalk, talc, kaolin, starch and derivatives thereof, gums, colloidal silicon dioxide, sodium polyacrylate, chemically modified magnesium aluminium silicate, hydrated aluminium silicate, carboxyvinyl polymer, sodium carboxymethyl cellulose, ethylene glycol monostearate;

15 gelling or swelling agents, such as pectin, gelatin and derivatives thereof, cellulose derivatives such as methyl cellulose, carboxymethyl cellulose or oxidised cellulose, cellulose gum, guar gum, acacia gum, karaya gum, tragacanth gum, bentonite, agar, alginates, carbomer, gelatine, bladderwrack, ceratonia, dextran and derivatives thereof, ghatti gum, hectorite, ispaghula husk, xanthan gum;

20 polymers, such as polylactic acid or polyglycolic acid polymers or copolymers thereof, paraffin, polyethylene, polyethylene oxide, polyethylene glycol, polypropylene glycol, polyvinylpyrrolidone;

25 surfactants, such as non-ionic surfactants, e.g. glycol and glycerol esters, macrogol ethers and esters, sugar ethers and esters, such as sorbitan esters, ionic surfactants, such as amine soaps, metallic soaps, sulfated fatty alcohols, alkyl ether sulfates, sulfated oils, and ampholytic surfactants and lecithins;

30 buffering agents, such as sodium, potassium, aluminium, magnesium or calcium salts (such as the chloride, carbonate, bicarbonate, citrate, gluconate, lactate, acetate, gluceptate or tartrate).

Furthermore, it is obvious that in the use according to the invention for the preparation of medicaments or dietary supplements, the above mentioned compositions may be mixed
35 with additives such as surfactants, solvents, thickeners, stabilisers, preservatives, antioxi-

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
DIRECCIÓN DE NUEVAS CREACIONES

2020
Bogotá, D.C.,

Abogado
EMILIO FERRERO
(Apoderado)

ASUNTO	Radicación	06128572
	Trámite	002
	Evento	001
	Actuación	430
	Oficio	05569
	Folios	022

Patente de Invención ☒ Patente de Modelo de Utilidad ☐

Vía Nacional ☐

Vía PCT (fase nacional) ☒ Cap. I ☐ Cap. II ☒

No. Sol. Internacional PCT/EP2005/006710
Fecha de Presentación Internacional 21-06-2005

Como resultado del examen de fondo, realizado con fundamento en el artículo 45 de la Decisión 486 de la Comisión de la Comunidad Andina, se le comunica:

1. Documentos estudiados:

1.1. Descripción: (Folios: 13 a 27) como se radicó inicialmente.

1.2. Reivindicaciones: 1 a 24 (Folios: 28 a 30) como se radicó inicialmente. Modificadas 1 a 23 (Folios: 45 a 49). Modificadas 1 a 30 (81 a 84).

1.3. Prioridad: 22/06/2004 DE 102004030044.5.

2. Análisis de la Prioridad:

La prioridad de la presente solicitud corresponde al objeto reivindicado.

3. Objeto de la invención:

La presente solicitud se titula: "Agente que forma oleogel que contiene triterpeno, oleogel que contiene triterpeno y método para producir un oleogel que contiene triterpeno".

El objeto de la presente solicitud se refiere a un formador de oleogel, un oleogel con ese formador de gel y un método para producir un oleogel.

De acuerdo con la descripción, los geles son sistemas dispersos finos consistentes de una fase líquida y una fase sólida, en el cual la fase sólida forma una estructura tridimensional cohesiva y ambas fases se compenetrán completamente. Se hace la diferencia entre los geles hidrófilos y los geles hidrófobos. Estos últimos se designan como oleogeles. Los oleogeles se basan en un líquido no polar, por ejemplo un aceite, una cera o una parafina, al cual se le agrega un formador de gel para obtener las propiedades físicas deseadas.

En el capítulo reivindicatorio se reclama lo siguiente:

Reivindicaciones 1 a 15 (folios: 81 y 82): Un oleogel que comprende:

- Un líquido no polar en una fracción entre 80 y 99% en peso con base en el peso total del gel
- Por lo menos un triterpeno altamente dispersado que tiene un tamaño de partícula promedio menor a 50 μm como un agente formador de oleogel en una fracción entre 1% y 20% en peso, con base en el peso total del gel.

Reivindicaciones 16 a 30 (folios: 82 a 84): Un método para la producción de un oleogel, que comprende una mezcla de los siguientes ingredientes:

Un líquido no polar en una fracción entre 80 y 99% en peso con base en el peso total del gel

- Al menos un triterpeno altamente dispersado que tiene un tamaño de partícula promedio menor a 50 μm como un agente formador de oleogel en una fracción entre 1% y 20% en peso, con base en el peso total del gel.

El problema planteado en esta solicitud es la necesidad de oleogeles que se calcinen sin formar cenizas.

La solución propuesta por la presente solicitud consiste en un formador de oleogel farmacéuticamente activo y que se calcina sin formar cenizas.

El objeto de la solicitud definido anteriormente se clasificó en la IPC A61K 9/06, A61K 7/48.

4. De la solicitud de Patente

4.1. Reivindicaciones (artículo 30 D 486)

De acuerdo con lo revelado en el capítulo reivindicatorio, la reivindicación 11 (folios: 46 y 47) no es concisa por cuanto no menciona específicamente los componentes del oleogel al que se refiere, sino que dice de manera general que contiene "un líquido no polar" y "triterpeno".

El método de la reivindicación 17 (folios: 47 y 48) no especifica las etapas o pasos del mismo, mencionando las variables que intervienen en él como por ejemplo: temperatura, velocidad de agitación o de mezclado, humedad, etc.

5. Análisis de la(s) Oposición(es): (artículo 43 D. 486)

No se presentaron oposiciones al objeto reivindicado.

6. Determinación del Estado de la Técnica:

La fecha que se ha tenido en cuenta para determinar el Estado de la Técnica es:

Fecha de presentación de la solicitud prioritaria 22-06-2004.

Teniendo en cuenta la fecha indicada, se buscaron documentos del estado de la técnica relacionados, con fecha de publicación anterior a esta.

Se encontró como anterioridades que pueden afectar la patentabilidad del objeto de la presente solicitud:

Nº	Documento	Título	Fecha de Publicación
D1	US 2003/0087789	Emulsion containing a plant extract, method for producing said emulsion and for obtaining a plant extract	8 de mayo de 2003
D2	WO 98/34603	Use of betulin and analogs thereof to treat herpesvirus infection	13 de agosto de 1998
D3	US 2001/0038878	Fat blebs with crystal modifiers	8 de noviembre de 2001
D4	WO 01/03712	Composition containing extracts of Butyrospermum parkii and the use as medicament or dietary supplement	18 de enero de 2001

7. Análisis de patentabilidad (artículo 14 D486)**7.1. Nivel inventivo (artículo 18 D486)**

La presente Solicitud de Patente reivindica lo siguiente: Un oleogel que comprende:
- Un líquido no polar en una fracción entre 80 y 99% en peso con base en el peso total del gel

- Por lo menos un triterpeno altamente dispersado que tiene un tamaño de partícula promedio menor a 50 µm como un agente formador de oleogel en una fracción entre 1% y 20% en peso, con base en el peso total del gel.

Un método para la producción de un oleogel, que comprende una mezcla de los siguientes ingredientes:

Un líquido no polar en una fracción entre 80 y 99% en peso con base en el peso total del gel

- Al menos un triterpeno altamente dispersado que tiene un tamaño de partícula promedio menor a 50 µm como un agente formador de oleogel en una fracción entre 1% y 20% en peso, con base en el peso total del gel.

La anterioridad US 2003/0087789 (folios: 87 a 90): se relaciona con una emulsión que contiene un extracto de una planta, método para la producción de dicha emulsión y para obtener el extracto. El extracto contiene triterpenos y derivados de los mismos y la emulsión contiene al menos un aceite y/o grasa y agua. Entre los terpenos se encuentran: betulina, ácido betulínico, ácido oleanólico, entre otros.

El documento WO 98/34603 (folios: 91 a 95) divulga derivados de betulina, composiciones farmacéuticas que comprende dichos derivados y el uso de derivados de betulina para preparar un medicamento. Entre las formas de dosificación de las composiciones se encuentran geles y ungüentos y se emplean como excipientes los comunes para este tipo de preparaciones como son los aceites, ácidos grasos, alcoholes grasos, celulosas modificadas.

La anterioridad US 2001/0038878 (folios: 96 a 103) se relaciona con combinaciones de aceites vegetales y al menos los triterpenos ácido ursólico y ácido oleanólico.

El documento WO 01/03712 (folios: 99 a 103) menciona composiciones de triterpenos formulados en forma de ungüento, gel, emulsión. Entre los emolientes empleados se encuentran los aceites vegetales.

Estos documentos mencionan varias formulaciones de oleogeles que comprenden un líquido no polar como por ejemplos los aceites vegetales, y por lo menos un triterpeno, tal como se menciona en la presente solicitud. En cuanto al tamaño de partícula de estos componentes, es obvio para una persona medianamente versada en la materia que éstos deban ir en un tamaño adecuado para la formulación requerida, además, vale la pena recordar que el tamaño de partícula es una característica física que no le confiere nivel inventivo a una composición; de igual manera, las composiciones se deben caracterizar por sus componentes en sí y no por el tamaño de éstos ni sus cantidades.

El problema técnico planteado en esta solicitud: la necesidad de oleogeles que se calcinen sin formar cenizas, se había resuelto previamente mediante formulaciones de oleogeles que contienen triterpenos ya conocidos(as). Por esta razón se considera que los componentes de los oleogeles reivindicadas en la presente solicitud son evidentes para una persona medianamente versada en la materia.

La(s) reivindicación(es) 1 a 30 de esta solicitud no menciona(n) una característica que conceda un efecto inesperado o especial a las composiciones, que pueda considerarse como un aporte a la técnica, así que son obvios(as) para una persona versada en la materia.

Además, puesto que D1, D2, D3 y D4 divulgaban previamente composiciones de triterpenos en forma de oleogel (folios: 87 a 103), una persona conocedora de la materia motivada por tal sugerencia lograría el objeto de esta solicitud oleogel que comprende un líquido no polar y por lo menos un triterpeno; de manera que para una persona medianamente versada en la materia sería obvio utilizar estos documentos. Por lo cual puede no haber Nivel Inventivo.

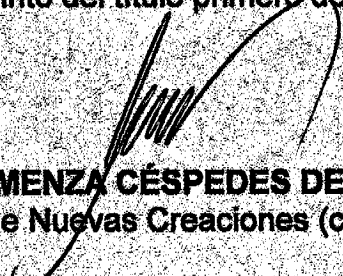
8. Conclusión:

Los requisitos de patentabilidad de la presente solicitud se encuentran afectados así:

Nº	Documento Nº	Reivindicaciones afectadas	Requisito que afecta
D1	US 2003/0087789	1 a 30	Nivel Inventivo
D2	WO 98/34603	1 a 30	Nivel Inventivo
D3	US 2001/0038878	1 a 30	Nivel Inventivo
D4	WO 01/03712	1 a 30	Nivel Inventivo

En cumplimiento del artículo 45 de la Decisión 486 de la Comisión de la Comunidad Andina, se le indica que debe dar respuesta dentro del término de sesenta días contados a partir de la fecha de la notificación de la presente comunicación. En caso de no dar respuesta al presente requerimiento o si a pesar de la respuesta subsistieran los impedimentos para la concesión, se denegará la patente.

Notifíquese el presente oficio conforme a lo dispuesto en el numeral 5.2, literal e), del capítulo quinto del título primero de la Circular Única Nº 10 de 2001.


ALIX CARMENZA CÉSPEDES DE VERGEL
Directora de Nuevas Creaciones (c)

El anterior requerimiento fue notificado por fijación en lista, de fecha 30 ABR. 2006

CONCEPTO TÉCNICO No. 1606	EXAMINADOR TÉCNICO Código No. 202005
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