

Señor Jefe
Dirección de Nuevas Creaciones
Superintendencia de Industria y Comercio
E. S. D.

Referencia: Solicitud de Privilegio para Patente de invención
Título: Hoja para aplicación cutánea que tiene un soporte y contiene vitamina E o un éster de la misma y su proceso de fabricación
Solicitante: BIO.LO.GA. S.R.L.
Exp. No.: 15-265.540
Asunto: Complemento de información

JESÚS M. MÉNDEZ BERMÚDEZ, identificado con cédula de ciudadanía No. 13.491.525 y con Tarjeta Profesional de Abogado No. 99.678 expedida por el Consejo Superior de la Judicatura, actuando como apoderado de la sociedad **BIO.LO.GA. S.R.L.**, por medio del presente escrito presento complemento de información relacionado con la respuesta al requerimiento No. 9490 de septiembre 9 de 2016.

1. En las reivindicaciones

Con el objeto de atender a la observación hecha por su Despacho con respecto a las reivindicaciones, Manifiesto lo siguiente:

En primer lugar, presento un nuevo capítulo de reivindicaciones en donde en lo posible y razonable se han efectuado las modificaciones necesarias siempre teniendo en cuenta no ampliar el objeto originalmente presentado.

En cuanto a la objeción presentada a la reivindicación 1, donde se manifiesta que no se definen las concentraciones de los excipientes y activos de la hoja, y además usar los nombres IUPA o DCI y su proporción, se ha corregido y modificado el capítulo de reivindicaciones para solucionar ese problema.

La reivindicación 10 se ha modificado para eliminar la aclaración “nomenclatura INCI” atendiendo así a la objeción hecha por su Despacho.

2. Análisis de la patentabilidad.

El examinador ha citado los documentos D1 US 4.838.253 denominado “Silicone gel coated permeable wound dressing”, del 13 de junio de 1989 y D2 US 6.495.158 denominado “Acne patch” del 17 de diciembre de 2002. De acuerdo con sus argumentos basados en la combinación de estos dos documentos D1 y D2, la materia reclamada no tiene nivel inventivo; queremos enfatizar o destacar que la combinación de D1 y D2 no conduce a la hoja para aplicación cutánea de acuerdo con la reivindicación 1, porque D1 no divulga un espesor menor a o igual a 2,0 mm y no enseña que la capa sólida de elastómero de silicona contiene un modificador de elasticidad que consiste de un triglicérido como se definió en la reivindicación 1. Aunque D2 divulga un parche adhesivo que comprende un respaldo flexible y una formulación terapéutica que incluye acetato de vitamina E, en donde el respaldo tiene un espesor de 0,025-1.25, sin

embargo, D2 es completamente silencioso con respecto a la posible presencia de un modificador de elasticidad como se definió en la reivindicación 1.

La presencia de un modificador de elasticidad como se definió en la reivindicación 1 en relación con el espesor definido en la reivindicación 1 es crucial para mejorar la conformabilidad de la hoja y para facilitar su remoción, como se reconoció en la IPRP (Ver el punto 1.3 de la IPRP adjunta).

Por lo tanto, podemos afirmar que una persona versada en la materia, aún si esta modificara la hoja descrita en D1 de acuerdo con las enseñanzas contenidas en D2, no hubiera llegado a obtener la hoja de acuerdo con la presente invención, porque la hoja así obtenida le hubiera faltado el modificador de elasticidad que es fundamental para asegurar el comportamiento de la hoja descrita de acuerdo con la reivindicación 1 de la presente invención. Así, la combinación de D1 y D2 no producen la presente invención de una manera evidente y por lo tanto la presente reivindicación 1 si tiene nivel inventivo en vista de D1 y D2.

Con base en lo anteriormente expuesto y resueltas cada una de las objeciones presentadas por el examinador, creemos que la presente invención cumple con los requisitos de patentabilidad exigidos por la normatividad vigente y en consecuencia es merecedora de protección por medio de patente de invención.

Pido, por lo tanto, de manera respetuosa, a su Despacho continuar con el trámite establecido y otorgar la patente a la presente solicitud.

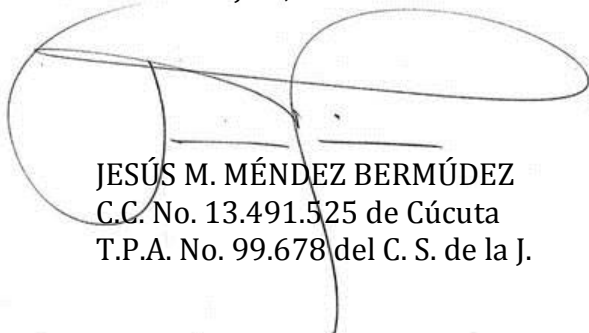
ANEXOS

1. Nuevo capítulo reivindicatorio
2. Recibo de pago por concepto modificaciones y correcciones a solicitudes en trámite.
3. Copia del IPRP

NOTIFICACIONES

Recibiré notificaciones en la Secretaria de este Despacho y en mi oficina, ubicada en la Calle 83ª No. 23-90 de esta ciudad.

Del Señor Jefe,



JESÚS M. MÉNDEZ BERMÚDEZ
C.C. No. 13.491.525 de Cúcuta
T.P.A. No. 99.678 del C. S. de la J.

REIVINDICACIONES

1. Una hoja para aplicación cutánea que comprende una capa de soporte elaborada de tela tejida de manera suelta incrustada en una capa sólida de elastómero de silicona reticulada, que consiste de un polisiloxano sustituido con vinilo reticulado con un polialquilhidrosiloxano, que tiene dispersa en ella vitamina E o un éster de la misma seleccionada del grupo que consiste de acetato, n-propionato y linoleato de vitamina E, en donde dicha capa de elastómero de silicona tiene un espesor menor que o igual a 2,0 mm y dicha capa sólida de elastómero de silicona tiene además disperso en ella un modificador de elasticidad seleccionado del grupo que consiste de triglicérido caprílico/cáprico, triglicérido caprílico/cáprico/esteárico y triglicérido caprílico/cáprico/mirístico/esteárico, y en donde dicho elastómero de silicona reticulada en dicha capa sólida está presente en una cantidad que es mayor a la de la vitamina E o un éster de la misma y dicho modificador de elasticidad en dicha capa sólida, y dicho modificador de elasticidad está presente en una cantidad menor a la de la vitamina E o un éster de la misma, dicha vitamina E o un éster de la misma está presente en una cantidad comprendida entre 2% y 40% en peso del peso de dicho elastómero de silicona y dicho modificador de elasticidad está presente en una cantidad entre 1 a 3% en peso del peso

de dicho elastómero de silicona.

2. La hoja de acuerdo a la reivindicación 1, en donde la tela tejida de manera suelta es gasa, particularmente una gasa de algodón.

3. La hoja de acuerdo a la reivindicación 1, en donde el éster de vitamina E es acetato de alfa-tocoferilo.

4. La hoja de acuerdo con cualquiera de las reivindicaciones 1 a 3, en donde la vitamina E o éster de la misma está contenida en la capa de elástica en una cantidad comprendida entre 5% y 30% en peso del peso de la capa elástica.

5. La hoja de acuerdo las reivindicaciones precedentes, en donde el triglicérido de ácidos grasos C₈-C₁₈ saturados es triglicérido caprílico/cáprico.

6. La hoja de acuerdo con cualquiera de las reivindicaciones 1 a 7, en donde la capa de elastómero de silicón tiene un espesor de entre 0-2 y 1.5 mm.

7. La hoja de acuerdo con las reivindicaciones precedentes, en donde la capa elástica es un copolímero de Bis-Vinil-Dimeticona/Dimeticona.

8. Un proceso para la producción de una hoja para aplicación cutánea de acuerdo con cualquiera de las reivindicaciones 1 a 10, que comprende los pasos de:

a) dispersar a temperatura ambiente y bajo agitación la vitamina E o su éster seleccionado del grupo que

consiste de acetato, n-propionato y linoleato de vitamina E y el triglicérido de ácidos grasos C_8-C_{18} saturados en un polisiloxano sustituido con vinilo, en una cantidad igual a 3.8-84-4% y 2-9-21.1% en peso del polisiloxano sustituido con vinilo,

b) adicionar, bajo agitación, un polialquilhidrosiloxano en una relación en peso con respecto al polisiloxano sustituido con vinilo que varía de 0.9:1.0 a 1.1:1.0, de manera preferente 1:1, obteniendo una dispersión homogénea;

c) depositar en la capa de soporte elaboradora de tela tejida de manera suelta la dispersión homogénea en una capa con un espesor de 0.2-2.0 mm y dejándola a temperatura ambiente durante un tiempo suficiente para obtener la formación de la hoja, preferentemente durante 12-2 horas.

9. Un proceso para la producción de una hoja para la aplicación cutánea que comprende una capa de soporte elaborada de tela tejida de manera suelta incrustada en una capa elástica de polisiloxano sustituido con vinilo, reticulado con un polialquilhidrosiloxano que incorpora vitamina E o un éster de la misma seleccionado del grupo que consiste de acetato, n-propionato y linoleato de vitamina E, en donde dicha capa elástica tiene un espesor menor que o igual a 2.0 mm, la capa elástica contiene un modificador de elasticidad seleccionado del grupo que consiste de

triglicérido caprílico/cáprico, triglicérido caprílico/cáprico/esteárico y triglicérido caprílico/cáprico/mirístico/esteárico, el proceso que comprende los pasos de:

a) dispersar a temperatura ambiente y en tanto que se agita la vitamina E o su éster y el triglicérido de ácidos grasos C_8-C_{18} saturados en un polisiloxano sustituido con vinilo, en una cantidad igual a 3.8-84-4% y 2.9-21.1% en peso del polisiloxano sustituido con vinilo,

b) adicionar, nuevamente en tanto que se agita, un polialquilhidrosiloxano en una relación en peso con respecto al polisiloxano sustituido con vinilo que varía de 0.9:1.0 a 11:10, preferentemente 1:1, obteniendo una dispersión homogénea;

c) depositar en la capa de soporte elaborada de tela tejida de manera suelta la dispersión homogénea en una capa con un espesor de 0.2-2.0 mm y dejándola a temperatura ambiente durante un tiempo suficiente para obtener la formación de la hoja, preferentemente durante 12-2 horas.

10. El proceso de acuerdo a la reivindicación 8 o 9, en donde el polisiloxano sustituido con vinilo es Bis-Vinil-Dimeticona y el polialquilhidrosiloxano es hidrógeno-dimeticona.

11. El proceso de acuerdo con cualquiera de las reivindicaciones 8 a 10, en donde en el paso a) el acetato de vitamina E se dispersa en el polisiloxano sustituido con

vinilo en una cantidad de entre 7.5-45% en peso del peso del polisiloxano sustituido con vinilo.

12. El proceso de acuerdo con cualquiera de las reivindicaciones 8 a 11, en donde la capa de soporte elaborada de tela tejida de manera suelta es una gasa de algodón.

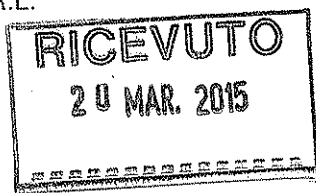
PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

To:

BOTTI & FERRARI S.R.L.
Via Cappellini, 11
I-20124 Milano
ITALIE



NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL PRELIMINARY
REPORT ON PATENTABILITY
(PCT Rule 71.1)

Date of mailing
(day/month/year)

18.03.2015

Applicant's or agent's file reference
PAN016BWO

IMPORTANT NOTIFICATION

International application No.
PCT/EP2014/000979

International filing date (day/month/year)
11.04.2014

Priority date (day/month/year)
06.05.2013

Applicant
BIO.LO.GA. S.r.l.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary report on patentability and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.
4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary report on patentability. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international
preliminary examining authority:



European Patent Office P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk - Pays Bas
Tel. +31 70 340 - 2040
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Authorized Officer

Miklos, Kamila

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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PAN016BWO		FOR FURTHER ACTION		See Form PCT/IPEA/416
International application No. PCT/EP2014/000979		International filing date (day/month/year) 11.04.2014		Priority date (day/month/year) 06.05.2013
International Patent Classification (IPC) or national classification and IPC INV. A61L15/44				
Applicant BIO.LO.GA. S.r.l.				
1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36. 2. This REPORT consists of a total of <u>5</u> sheets, including this cover sheet. 3. This report is also accompanied by ANNEXES, comprising: a. ☐ (sent to the applicant and to the International Bureau) a total of sheets, as follows: ☐ sheets of the description, claims and/or drawings which have been amended and/or sheets containing rectifications authorized by this Authority, unless those sheets were superseded or cancelled, and any accompanying letters (see Rules 46.5, 66.8, 70.16, 91.2, and Section 607 of the Administrative Instructions). ☐ sheets containing rectifications, where the decision was made by this Authority not to take them into account because they were not authorized by or notified to this Authority at the time when this Authority began to draw up this report, and any accompanying letters (Rules 66.4bis, 70.2(e), 70.16 and 91.2). ☐ superseded sheets and any accompanying letters, where this Authority either considers that the superseding sheets contain an amendment that goes beyond the disclosure in the international application as filed, or the superseding sheets were not accompanied by a letter indicating the basis for the amendments in the application as filed, as indicated in item 4 of Box No. I and the Supplemental Box (see Rule 70.16(b)). b. ☐ (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see paragraph 3bis of Annex C of the Administrative Instructions).				
4. This report contains indications relating to the following items: ☒ Box No. I Basis of the report ☐ Box No. II Priority ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability ☐ Box No. IV Lack of unity of invention ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement ☐ Box No. VI Certain documents cited ☐ Box No. VII Certain defects in the international application ☐ Box No. VIII Certain observations on the international application				
Date of submission of the demand		Date of completion of this report		
22.01.2015		18.03.2015		
Name and mailing address of the international preliminary examining authority:  European Patent Office P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Fax: +31 70 340 - 3016		Authorized officer Siebum, Bastiaan Telephone No. +31 70 340-9174		



**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/EP2014/000979

Box No. I Basis of the report

1. With regard to the **language**, this report is based on
- ☒ the international application in the language in which it was filed
 - ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of:
 - ☐ international search (under Rules 12.3(a) and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4(a))
 - ☐ international preliminary examination (under Rules 55.2(a) and/or 55.3(a) and (b))
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-15 as originally filed

Claims, Numbers

1-22 as originally filed

- ☐ a sequence listing - see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages
- ☐ the claims, Nos.
- ☐ the drawings, sheets/figs
- ☐ the sequence listing (*specify*):
- ☐ any table(s) related to sequence listing (*specify*):

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since either they are considered to go beyond the disclosure as filed, or they were not accompanied by a letter indicating the basis for the amendments in the application as filed, as indicated in the Supplemental Box (Rules 70.2(c) and (c-bis)):

- ☐ the description, pages
- ☐ the claims, Nos.
- ☐ the drawings, sheets/figs
- ☐ the sequence listing (*specify*):

5. ☐ This report has been established:

- ☐ taking into account the rectification of an obvious mistake authorized by or notified to this Authority under Rule 91 (Rules 66.1(d-bis) and 70.2(e)).
- ☐ without taking into account the rectification of an obvious mistake authorized by or notified to this Authority under Rule 91(Rules 66.4bis and 70.2(e)).

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/EP2014/000979

6. ☒ With regard to top-up searches (Rules 66.1 ter and 70.2(f)):
- ☒ A top-up search was carried out by this Authority on 06.03.2015 (all discovered documents are listed in the Supplemental Box Relating to Top-up Search).
 - ☐ Additional relevant documents have been discovered during the top-up search.
 - ☐ No top-up search was carried out by this Authority.
7. ☐ Supplementary international search report(s) from Authority(ies) has/have been received and taken into account in establishing this report (Rule 45bis.8(b) and (c)).

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	<u>1-22</u>
	No: Claims	
Inventive step (IS)	Yes: Claims	<u>1-22</u>
	No: Claims	
Industrial applicability (IA)	Yes: Claims	<u>1-22</u>
	No: Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

1 **Re Item V**

1.1 Reference is made to the following documents:

- | | |
|----|--------------------------------|
| D1 | EP 0 597 340 A1 (1994-05-18) |
| D2 | US 5 919 476 A (1999-07-06) |
| D3 | EP 1 186 290 A2 (2002-03-13) |
| D4 | US 2011/313372 A1 (2011-12-22) |
| D5 | WO 00/02535 A1 (2000-01-20) |

1.2 **Novelty**

The subject-matter of claim 1-22 is new in the sense of Article 33(2) PCT.

Document D1 discloses a sheet for cutaneous application comprising a support layer made of loosely woven fabric embedded in a layer of silicone elastomer incorporating vitamin E wherein said silicone layer has a thickness of 3.0 mm and comprises low molecular weight silicone polymer or specifically dimethylvinylpolysiloxane as elasticity modifier (D1: examples and col.2 l.44-58). D1 does not disclose a thickness of less than or equal to 2.0 mm nor a triglyceride of saturated C8-C18 fatty acids.

Documents D2 and D3 disclose sheets for cutaneous application comprising a support layer embedded in a layer of silicone elastomer incorporating vitamin E (D2: cl.14 and col.4 l. 53-62 and D3: col.4 par.[0027] and [0029]), however both do not disclose a triglyceride of saturated C8-C18 fatty acids is used as elasticity modifier.

Document D4 discloses sheets for cutaneous application comprising a release matrix, which can be silicone polymer wherein the elasticity modifier can be a triglyceride of C8-C18 fatty acids, specifically caprylic acid or capric acid (D4: par.[0081]). D4 does not disclose vitamin E as active compound in combination with a silicone polymer.

Document D5 discloses an oil for application of vitamin E to the skin, wherein the vitamin E derivative can also be an ester such as an acetate (D5: cl.22 and 23). The composition of D5 does not comprise a silicone polymer layer, nor a support layer.

1.3 **Inventive step**

The subject-matter of claim 1-22 involves an inventive step (Article 33(3) PCT).

Document D1 is regarded as being the closest prior-art.

The subject-matter of claim 1 differs from D1 in that the silicone elastomer layer has a thickness of less than or equal to 2.0 mm and in that the elasticity modifier consists of a triglyceride of saturated C8-C18 fatty acids.

The thickness and the elasticity modifier choice are both aimed at improving conformability of the sheet and facilitating removal (p.3 l.3-9). The previous allegation by the examiner that these results are also obtained by D1 are withdrawn in view of the comparative results. These show an improvement in extensibility and permanent set and illustrate improved conformability.

Thus, the objective technical problem is considered as to provide a sheet of silicone elastomer comprising vitamin E and an elasticity modifier, applied to a woven fabric as backing, wherein the sheet has improved conformability to the users skin, resulting in improved adherence and easier removal afterwards.

Thicknesses of 2 mm for a flexible sheet (D2: cl.21) and 1.0-1.2 mm due to convenience and costs (D3: col.4 par.[0025]) have been shown in the prior-art, but not in combination with the triglyceride of saturated C8-C18 fatty acids to improve conformability. Triglycerides of saturated C8-C18 fatty acids have been used as plasticizer in a similar compositions or articles (D4: par.[0081]), but not together with the selected thickness and not to improve conformability. There is no indication in the prior-art or in general knowledge that use such a thin gel layer together with this specific elasticity modifier would lead to superiour conformability.

1.4 Industrial applicability

The subject-matter of claims 1-22 is considered to be industrial applicable and is therefore considered to satisfy the criteria set forth in Article 33(4) PCT.

The
United
States
of
America



**The Director of the United States
Patent and Trademark Office**

Has received an application for a patent for a new and useful invention. The title and description of the invention are enclosed. The requirements of law have been complied with, and it has been determined that a patent on the invention shall be granted under the law.

Therefore, this

United States Patent

Grants to the person(s) having title to this patent the right to exclude others from making, using, offering for sale, or selling the invention throughout the United States of America or importing the invention into the United States of America, and if the invention is a process, of the right to exclude others from using, offering for sale or selling throughout the United States of America, or importing into the United States of America, products made by that process, for the term set forth in 35 U.S.C. 154(a)(2) or (c)(1), subject to the payment of maintenance fees as provided by 35 U.S.C. 41(b). See the Maintenance Fee Notice on the inside of the cover.

Michelle K. Lee

Director of the United States Patent and Trademark Office

MAINTENANCE FEE NOTICE

If the application for this patent was filed on or after December 12, 1980, maintenance fees are due three years and six months, seven years and six months, and eleven years and six months after the date of this grant, or within a grace period of six months thereafter upon payment of a surcharge as provided by law. The amount, number and timing of the maintenance fees required may be changed by law or regulation. Unless payment of the applicable maintenance fee is received in the United States Patent and Trademark Office on or before the date the fee is due or within a grace period of six months thereafter, the patent will expire as of the end of such grace period.

PATENT TERM NOTICE

If the application for this patent was filed on or after June 8, 1995, the term of this patent begins on the date on which this patent issues and ends twenty years from the filing date of the application or, if the application contains a specific reference to an earlier filed application or applications under 35 U.S.C. 120, 121, 365(c), or 386(c), twenty years from the filing date of the earliest such application ("the twenty-year term"), subject to the payment of maintenance fees as provided by 35 U.S.C. 41(b), and any extension as provided by 35 U.S.C. 154(b) or 156 or any disclaimer under 35 U.S.C. 253.

If this application was filed prior to June 8, 1995, the term of this patent begins on the date on which this patent issues and ends on the later of seventeen years from the date of the grant of this patent or the twenty-year term set forth above for patents resulting from applications filed on or after June 8, 1995, subject to the payment of maintenance fees as provided by 35 U.S.C. 41(b) and any extension as provided by 35 U.S.C. 156 or any disclaimer under 35 U.S.C. 253.



US009408827B2

(12) United States Patent
Panin**(10) Patent No.: US 9,408,827 B2**
(45) Date of Patent: *Aug. 9, 2016**(54) SHEET FOR CUTANEOUS APPLICATION
CONTAINING VITAMIN E OR AN ESTER
THEREOF****(71) Applicant: IneSalus Corp., Las Vegas, NV (US)****(72) Inventor: Giorgio Panin, Rovigo (IT)****(73) Assignee: BIO.LO.GA S.R.L., Conegliano (TV)
(IT)****(*) Notice:** Subject to any disclaimer, the term of this
patent is extended or adjusted under 35
U.S.C. 154(b) by 0 days.This patent is subject to a terminal dis-
claimer.**(21) Appl. No.: 13/901,963****(22) Filed: May 24, 2013****(65) Prior Publication Data**

US 2014/0328885 A1 Nov. 6, 2014

(30) Foreign Application Priority Data

May 6, 2013 (IT) MI2013A0732

(51) Int. Cl.**A61K 31/355** (2006.01)**A61L 15/26** (2006.01)**A61L 15/44** (2006.01)**C08L 83/04** (2006.01)**(52) U.S. Cl.**CPC **A61K 31/355** (2013.01); **A61L 15/26**
(2013.01); **A61L 15/44** (2013.01); **A61L**
2300/428 (2013.01)**(58) Field of Classification Search**CPC ... **A61K 9/7007**; **A61K 47/34**; **A61K 9/0014**;
A61K 31/355; **A61L 15/26**; **A61L 15/44**;
A61L 2300/428

See application file for complete search history.

(56)**References Cited****U.S. PATENT DOCUMENTS**4,838,253 A * 6/1989 Brassington et al. 602/48
5,919,476 A 7/1999 Fischer
6,495,158 B1 * 12/2002 Buseman et al. 424/443
2010/0003201 A1 * 1/2010 Wahl 424/49
2010/0172856 A1 * 7/2010 Dias et al. 424/70.12
2011/0313372 A1 12/2011 Eifler et al.**FOREIGN PATENT DOCUMENTS**EP 0597340 5/1994
EP 1186290 3/2002
WO 00/02535 1/2000
WO WO 2004100906 A2 * 11/2004**OTHER PUBLICATIONS**Wikipedia (http://en.wikipedia.org/wiki/Coconut_oil, last visit on
Mar 4, 2015).*European Search Report corresponding to IT priority application
MI2013A000732.International Search Report mailed Jul. 14, 2014, which was issued in
connection with a related PCT International Application No. PCT/
EP2014/000979 (4 pages).PCT International Preliminary Report on Patentability dated Mar 18,
2015, which was issued in a related PCT International Application
No. PCT/EP2014/000979, which co-pending U.S. Appl. No.
14/888,585, filed Nov. 2, 2015 is based upon (6 pages).

* cited by examiner

Primary Examiner — Ernst V Arnold*Assistant Examiner* — Kyung Sook Chang(74) *Attorney, Agent, or Firm* — Lucas & Mercanti, LLP**(57)****ABSTRACT**Sheet for cutaneous application comprising a support layer
made of loosely woven fabric embedded in a layer of silicone
elastomer incorporating vitamin E or an ester thereof,
wherein the layer of silicone elastomer has a thickness less
than or equal to 2.0 mm and the silicone elastomer contains an
elasticity modifier consisting of a triglyceride of saturated
C₈-C₁₈ fatty acids.**23 Claims, No Drawings**

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SHEET FOR CUTANEOUS APPLICATION CONTAINING VITAMIN E OR AN ESTER THEREOF

This application is a Non-Provisional Application which claims priority to and the benefit of Italian Application No. MI2013A000732 filed on May 6, 2013 the content of which is incorporated herein by reference in its entirety.

FIELD OF APPLICATION

The present invention relates to the sector of the pharmaceutical and cosmetics industry.

In particular the invention relates to a sheet based on silicone polymers and containing vitamin E or an ester thereof, intended for application on the skin in order to obtain a moisturizing and protective effect and/or prevent and treat various skin conditions.

PRIOR ART

For some time sheets based on silicone polymers used for the treatment of scars which are excessively visible, hypertrophic scars, scars due to burns, keloids and excessive keratinization of given skin areas, as well for obtaining a marked local moisturizing effect, have been known.

In particular, the patent application EP 0 597 340 describes a medication for skin disorders, such as keloids, desquamation and skin hypertrophy in closed wounds and bedsores, consisting of a sheet of crosslinked silicone material comprising interstices filled with a linear silicone polymer which contains an active substance, in particular vitamin E.

The patent EP 0 251 810 B1 describes a liquid-permeable dressing comprising one or more layers of an apertured support material, for example a gauze, coated with a quantity of crosslinked silicone sufficient for encapsulating the aforementioned support material. The crosslinked silicone is preferably an adhesive silicone gel or a non-adhesive silicone elastomer. The support material may be coated on one side with adhesive silicone gel and on the other side with non-adhesive silicone elastomer. This medication is used in particular for wounds and avoids the problem of adhesion to the wounds encountered with conventional dressings which use gauze and vaseline.

Also commercially available are sheets based on silicone polymers, such as the Sifravite® sheet made by the company Fresenius Kabi Italia S.r.l., based on the aforementioned patent EP 0 597 340 and containing vitamin E acetate, and the sheet Lipoplast® of the company Cereal's Italia, containing aleurone and vitamins A, C and E.

In both cases these consist of sheets characterized by a thickness of about 4-5 mm and provided with a light mesh on one of the two sides, in order to facilitate handling of the sheet, which must however be applied onto the skin with the side which is mesh-free.

These sheets, in particular in the skins areas which are exposed to friction, may wear and break easily.

The object of the present invention is to provide an adhesive sheet based on silicone polymers for cutaneous application, containing vitamin E or an ester thereof, which is thin and soft and consequently easier to handle and more easily adaptable to the skin surface onto which it is applied compared to the known sheets.

Such a sheet must at the same time be able to release vitamin E or an ester thereof to the skin and be suitable for use in the prevention and treatment of keloids and abnormal wound healing processes such as desquamation, exfoliation

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and hypertrophy, in the treatment of sunburn, in the protection of sensitive zones of the skin from contact with external agents of any kind (atmospheric, physical or mechanical) and in relaxing the skin by means of a deep moisturizing action.

SUMMARY OF THE INVENTION

The aforementioned object is achieved by providing a sheet comprising a support layer made of loosely woven fabric embedded in a layer of silicone elastomer, incorporating vitamin E or an ester thereof, wherein the layer of silicone elastomer has a thickness less than or equal to 2.0 mm and this silicone elastomer contains an elasticity modifier consisting of a triglyceride of saturated C₈-C₁₈ fatty acids.

The presence of the loosely woven fabric allows the sheet to be provided internally with a plurality of holes which allow air to pass through, creating a breathable bandage which ensures an optimum cutaneous micro-environment.

The reduced thickness of the sheet is such that it adheres perfectly to the skin, also at joints or in any case in skin areas which are not flat, and adheres thereto for a long time.

The triglyceride of saturated C₈-C₁₈ fatty acids helps make the sheet more elastic, increasing further its flexibility and capacity to adhere to the skin, and facilitates removal of the sheet from the skin, reducing or preventing any traumatic effect.

This triglyceride of saturated C₈-C₁₈ fatty acids is preferably selected from the group consisting of the following (INCI nomenclature): Caprylic/Capric Triglyceride, Caprylic/Capric/Stearic Triglyceride and Caprylic/Capric/Myristic/Stearic Triglyceride, and advantageously consists of Caprylic/Capric Triglyceride.

The aforementioned loosely woven fabric preferably consists of gauze, in particular cotton gauze.

The vitamin E may be used as d- α -tocopherol, as a mixture of the two enantiomers d and l of α -tocopherol, as a mixture of other tocopherols (β , γ , δ , ϵ , ζ , η) or as tocotrienols.

"Vitamin E ester" is understood as meaning an ester of vitamin E as defined above with a carboxylic acid of formula R-COOH, wherein R is an alkyl radical having 1 to 19 carbon atoms, or an alkenyl or alkynyl radical having 2 to 19 carbon atoms.

Preferably, the aforementioned ester is vitamin E acetate, n-propionate or linoleate.

Particularly preferred is the use of vitamin E acetate, in particular alpha-tocopheryl acetate.

Vitamin E or the ester thereof are typically contained in the layer of silicone elastomer in an amount comprised between 2% and 40%, preferably 5-30%, by weight of the weight of the silicone elastomer.

The content of Caprylic/Capric Triglyceride is preferably equal to 1-3% by weight of the weight of the silicone elastomer.

The thickness of the layer of silicone elastomer is preferably between 0.2 and 1.5 mm.

The sheet according to the present invention may be produced in various shapes, but generally has a quadrangular shape. Typically it is produced in the form of squares with a side size of 8-10 cm, but it obviously may be produced also in shapes and sizes which are different depending on the uses envisaged.

The aforementioned silicone elastomer preferably consists of a vinyl-substituted polysiloxane crosslinked with a polyalkylhydrosiloxane (i.e. a polysiloxane containing Si-H groups) and advantageously of Bis-Vinyl Dimethicone/Dimethicone Copolymer (INCI nomenclature).

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The sheet according to the present invention is produced using a process which comprises the steps of:

a) dispersing at room temperature and while stirring the vitamin E or its ester and the triglyceride of saturated C₈-C₁₈ fatty acids in a vinyl-substituted polysiloxane, in amounts equal, respectively, to 3.8-84.4% and 2.9-21.1% by weight of the vinyl-substituted polysiloxane;

b) adding, still while stirring, the polyalkyl hydrosiloxane in a weight ratio with respect to the vinyl-substituted polysiloxane ranging from 0.9:1.0 to 1.1:1.0, obtaining a homogeneous dispersion;

c) depositing on the support layer made of loosely woven fabric said homogeneous dispersion in a layer with a thickness of 0.2-2.0 mm and leaving it at room temperature for a time sufficient to obtain the formation of the sheet, preferably for 2-12 hours.

Preferably, the aforementioned vinyl-substituted polysiloxane is Bis-Vinyl Dimethicone (INCI nomenclature) and the aforementioned polyalkylhydrosiloxane is Hydrogen-Dimethicone (INCI nomenclature).

Preferably vitamin E acetate is used in an amount of 7.5-45% by weight of the weight of the vinyl-substituted polysiloxane.

Preferably the aforementioned support layer made of loosely woven fabric is a cotton gauze.

Preferably the aforementioned triglyceride of saturated C₈-C₁₈ fatty acids is selected from the group consisting of the following (INCI nomenclature): Caprylic/Capric Triglyceride, Caprylic/Capric/Stearic Triglyceride and Caprylic/Capric/Myristic/Stearic Triglyceride, and advantageously consists of Caprylic/Capric Triglyceride.

As mentioned above, the sheet according to the present invention is used for the following:

- preventing the formation of keloids and treating keloids which have already formed;
- preventing abnormal wound healing processes, such as desquamation, exfoliation and hypertrophy, and for treating them if they are already present;
- treatment of sunburn;
- relaxing the skin by means of its deep moisturizing action;
- protecting sensitive areas of the skin from contact with external agents of any nature (atmospheric, physical, chemical and mechanical).

The sheet may be applied using both its sides.

In order to ensure maximum hygiene during use of the sheet according to the present invention, the sheet is enclosed between two foils of transparent plastic material, for example polyethylene, and packaged inside multilayer bags, typically consisting of paper/polyethylene/aluminium or polyethylene/aluminium/polyethylene, and the package is sterilised. Preferably sterilisation is performed by means of irradiation with gamma rays, because this treatment does not alter the three-dimensional structure of the silicone elastomer, does not degrade the vitamin E or ester thereof, and does not adversely affect the quality of the fabric support layer.

The sheet is kept sterile until the package is opened and, following opening and removal of the plastic foils between which it is enclosed, it may be used again, i.e. applied, removed and applied again repeatedly for several days.

DETAILED DESCRIPTION OF A PREFERRED EMBODIMENT

The present invention will be further described with reference to an example of embodiment of the sheet according to the present invention provided purely by way of a non-limiting example.

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12.6 g of vitamin E acetate and 0.7 g of Caprylic/Capric Triglyceride were dispersed in 42.2 g of Bis-Vinyl Dimethicone while stirring at a low speed at room temperature for 10 minutes, until a homogeneous dispersion was obtained.

42.2 g of Hydrogen Dimethicone were added to the homogeneous dispersion thus obtained while stirring at a low speed at room temperature. The stirring was continued for 10 minutes, following which the fluid and homogeneous dispersion obtained was deposited on top of a strip of cotton gauze with 10 cm side size having square meshes with dimensions of 2 mm, said strip being passed through two rollers in order to ensure a homogeneous distribution of the fluid dispersion and then through two blades for cutting the top and bottom side until a height of 10 cm was obtained, in such a way as to form a layer with a thickness of 1.5 mm.

After a time period of about 10 hours, during which a crosslinking reaction between the Bis-Vinyl Dimethicone and the Hydrogen-Dimethicone occurred and was completed, sheets with a thickness of about 1.5 cm incorporating the cotton gauze were obtained.

Each sheet was enclosed in sandwich form between two square foils of polyethylene with a 11-cm side and packaged inside a bag of multilayer material (PE/ALU/PE).

The sheets thus packaged were finally sterilised with gamma rays using a minimum sterilising dose equal to 18.4 kGy.

The tolerability of the sheets according to the invention was evaluated by means of an in-vitro assay on models of reconstituted epidermis for evaluation of the cumulative irritation.

The assay in question was based on the In vitro Epiderm™ Skin Irritation Test (EPI-200-SIT) developed by the MatTek Corporation, which uses the model of reconstituted human epidermis Epi-200 EpiDerm™.

The assay consists in topical application of the material under testing on the reconstituted epidermis for contact times equal to or greater than 18 hours. The irritation potential is determined by means of evaluation of the cellular vitality using the MTT assay.

Further information for better defining the irritation potential was obtained from subsequent measurement of the following parameters:

- evaluation of the release, in the culture medium, of the lactate dehydrogenase (LDH), a cytoplasmic enzyme, release of which indicates loss of integrity of the cellular membrane;
- evaluation of the release, in the culture medium, of pro-inflammatory cytokine by means of ELISA (Enzyme Linked Immunosorbent Assay).

Conditions for Conducting the Assay for Evaluation of the Cellular Vitality

Tissue used: EPI-200-SIT EpiDerm™

Culture medium: EPI-100-MM-HCF-60

Incubation conditions: +37° C. in a 5% CO₂ atmosphere

Treatment with the sample:

continuous contact and incubation for 18 hours (single)

continuous contact and incubation for 7 days (double)

Application was carried out by applying about 1 cm² of sample (i.e. of the sheet according to the invention obtained as per the example given above) per insert.

Controls Performed for the First Evaluation (18 Hours):

Negative control after 18 hours: inserts not treated

Positive control: inserts treated with 0.5% SDS (Sodium Dodecylsulphate) in sterile water during 18 hours of incubation;

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Controls Performed for the 7-Day Evaluation:

Negative control: inserts not treated with the sample and kept for 7 days in the same incubation conditions as those treated with the sample.

Evaluation of the Cellular Vitality:

MTT assay: colorimetric determination of the vitality of the keratinocytes of the insert based on the reduction of the yellow tetrazolium salts (MTT) to blue formazan by mitochondrial dehydrogenases.

Evaluation of the Cytotoxicity by Means of Measurement of the Release of the Lactate Dehydrogenase (LDH) in the Culture Medium:

Evaluation in the culture medium obtained after the incubation period of the sample with the epidermis model. The culture medium is incubated with a specific reagent so as to allow quantitative determination of the lactate dehydrogenase at 490 nm.

Evaluation of the Release of IL-1 α in the Culture Medium:

Evaluation in the culture medium obtained after the period of incubation of the sample with EPI-200. The release is measured by means of specific ELISA.

Criteria for Interpretation of the Results of the Individual Assays Performed

Interpretation Criteria for Evaluation of the Cellular Vitality by Means of the MTT Assay:

Cumulative Irritation

Continuous Stimulation (Overnight Contact and Incubation)

Vitality (MTT)	Evaluation
<50%	irritant
≥50%	possible non-irritant, to be verified also after further evaluation

Interpretation Criteria for Evaluation of the Release of Pro-Inflammatory Cytokines in the Culture Medium in Relation to the LDH Values:

Variation with respect to the negative control	Evaluation
↑ LDH and ↑ cytokines	irritant
LDH unvaried and ↑ cytokines	mild irritant

Overall Criteria for Evaluation of the Assays

The classification of a product as "non irritant" means that the product applied on the reconstituted skin model does not reduce the cellular vitality thereof below the threshold value and does not result in a significant increase by the keratinocytes of inflammation mediators, induced by the irritating stimulus.

Non-irritant ingredient/finished product: absence of cytotoxicity, no significant increase in the release and genic expression of pro-inflammatory cytokines.

Mild irritant ingredient/finished product: absence of cytotoxicity, no significant increase in the release and genic expression of pro-inflammatory cytokines.

Severe irritant ingredient/finished product: presence of cytotoxicity

Results

The results obtained during the tests carried out for the two time periods considered in relation to the cellular vitality, release of LDH and IL-1 α are shown below.

The statistical analysis was carried out using the program GraphPad Instat version 3.0 for Windows 95 (GraphPad Software, San Diego, Calif., USA).

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The values of $p \leq 0.05$ recorded using the "Tukey Kramer Multiple Comparisons Test" were considered significant for the statistical comparisons of the 18-hour treatment and those recorded using the "Unpaired t test" for the comparisons of the 7-day treatment.

18-Hour Treatment Results

Evaluation of the Cellular Vitality by Means of MTT Assay

Table 1 shows the average values of OD (Optical Density) $\pm$ Standard Deviation (SD) obtained in the reading after continued stimulus. The values obtained for the positive control and for the sample are shown in relation to those obtained for the negative control, to which 100% vitality is attributed. A single insert was used for the sample.

TABLE 1

Treatment	Inserts	Average value of OD $\pm$ SD	Average value of the % vitality
1	Negative control	2.204 $\pm$ 0.018	100.00 $\pm$ 0.82
2	Negative control		
2	Positive control	0.185 $\pm$ 0.004	8.40 $\pm$ 0.17
3	Positive control		
3	Sample	2.158	97.90

Evaluation of the Release of Lactate Dehydrogenase (LDH) in the Culture Medium

Table 2 shows the results as follows:

3rd column: average values for release of LDH obtained for the controls and for the sample, expressed in Absorbency Units with the associated Standard Deviation (SD)

4th column: results of the statistical comparison in relation to the negative control

TABLE 2

Treatment	Culture medium derived from:	Average value $\pm$ SD	Statistical comparison
1	Negative control	0.147 $\pm$ 0.010	—
2	Negative control		
2	Positive control	1.414 $\pm$ 0.011	***
3	Positive control		
3	Sample	0.289 $\pm$ 0.069	insig.
3	Sample		

insig. insignificant variation

* $p < 0.05$ significant variation

** $p < 0.01$ very significant variation

*** $p < 0.001$ extremely significant variation

Evaluation of the Release of IL-1 α in the Culture Medium

Table 3 shows the average values, with the associated Standard Deviation (SD), for release of IL-1 α obtained in the reading for the sample and the controls expressed in pg/ml.

The statistical comparison of any increase in the release of IL-1 α is performed in relation to the negative control.

TABLE 3

Treatment	Culture medium derived from:	Average value $\pm$ SD	Statistical comparison
1	Negative control	9.8 $\pm$ 0.7	—
2	Negative control		
2	Positive control	108.5 $\pm$ 10.0	***
3	Positive control		
3	Sample	21.0 $\pm$ 1.7	insig.
3	Sample		

insig. insignificant variation

* $p < 0.05$ significant variation

** $p < 0.01$ very significant variation

*** $p < 0.001$ extremely significant variation

7-Day Treatment Results

Evaluation of the Cellular Vitality by Means of MTT Assay

Table 4 shows the average values of OD (Optical Density) $\pm$ Standard Deviation (SD) obtained in the reading after prolonged stimulus for 7 days. The values obtained for the sample are shown in relation to those obtained for the associated negative control, to which 100% vitality is attributed.

TABLE 4

Treatment	Inserts	Average value of OD $\pm$ SD	Average $\pm$ SD of the % vitality
1	Negative control	1.402 $\pm$ 0.040	100.00 $\pm$ 2.82
2	Negative control		
	Sample	2.116 $\pm$ 0.309	150.89 $\pm$ 22.04
	Sample		

Evaluation of the Release of the Lactate Dehydrogenase (LDH) in the Culture Medium

Table 5 shows the results as follows:

3rd column: average values of the release of LDH obtained for the control and for the sample, expressed in Absorbency Units with the associated Standard Deviation (SD)

4th column: Results of the statistical comparison in relation to the negative control.

TABLE 5

Treatment	Culture medium derived from:	Average value $\pm$ SD	Statistical comparison
1	Negative control	0.788 $\pm$ 0.008	—
2	Negative control		
	Sample	0.672 $\pm$ 0.044	insig.
	Sample		

insig. insignificant variation

* $p < 0.05$ significant variation

** $p < 0.01$ very significant variation

*** $p < 0.001$ extremely significant variation

Evaluation of the Release of IL-1 α in the Culture Medium

Table 6 shows the average values, with the associated Standard Deviation, for release of IL-1 α obtained in the reading for the sample and for the control expressed in pg/ml.

The statistical comparison of any increase in the release of IL-1 α is performed in relation to the negative control.

TABLE 6

Treatment	Culture medium derived from:	Average value $\pm$ SD	Statistical comparison
1	Negative control	10.6 $\pm$ 3.1	—
2	Negative control		
	Sample	14.3 $\pm$ 3.9	insig.
	Sample		

insig. insignificant variation

* $p < 0.05$ significant variation

** $p < 0.01$ very significant variation

*** $p < 0.001$ extremely significant variation

CONCLUSIONS

Test after 18 Hours' Incubation

The following conclusions may be reached with regard to evaluation of the results obtained.

Cumulative Irritation

% Vitality (MTT)	Evaluation
97.90	non irritant

The values for release of inflammatory response mediators, such as interleukin 1- α , do not differ significantly from those recorded for the negative control; this means that the sample does not induce a cutaneous inflammatory stimulus.

Test after 7 Day Incubation

Evaluation of the results obtained after 7 days' application shows that the inserts treated with the sample maintain an excellent cellular vitality value.

The values for release of interleukin 1- α do not differ significantly from those recorded for the negative control.

The data obtained suggest that the sample may be classified as a "skin non-irritant".

The product is perfectly tolerated even after 7 days continuous contact, with no modification of the parameters evaluated as indicators of cellular damage.

The invention claimed is:

1. A sheet for cutaneous application comprising a support layer made of loosely woven fabric embedded in a solid layer of cross-linked silicone elastomer having dispersed therein vitamin E or an ester thereof,

wherein said layer of silicone elastomer has a thickness less than or equal to 2.0 mm and said solid layer of silicone elastomer having further dispersed therein an elasticity modifier consisting of a triglyceride of saturated C₈-C₁₈ fatty acids, and

wherein said cross-linked silicone elastomer in said solid layer is present in an amount that is greater than said vitamin E or an ester thereof and said triglyceride in said solid layer, and said triglyceride is present in an amount less than said vitamin E or an ester thereof.

2. The sheet according to claim 1, wherein said loosely woven fabric is gauze.

3. The sheet according to claim 2, wherein said gauze is a cotton gauze.

4. The sheet according to claim 1, wherein said silicone elastomer incorporates an ester of vitamin E with a carboxylic acid of formula R-COOH, wherein R is an alkyl radical having 1 to 19 carbon atoms, or an alkenyl or alkynyl radical having 2 to 19 carbon atoms.

5. The sheet according to claim 4, wherein said ester of vitamin E is vitamin E acetate, n-propionate or linoleate.

6. The sheet according to claim 5, wherein said ester of vitamin E is alpha-tocopheryl acetate.

7. The sheet according to claim 1, wherein said vitamin E or ester thereof is dispersed in said layer of silicone elastomer in an amount comprised between 2% and 40%.

8. The sheet according to claim 1, wherein said vitamin E or ester thereof is dispersed in said layer of silicone elastomer in an amount comprised between 5% and 30%, by weight of the weight of the silicone elastomer.

9. The sheet according to claim 1, wherein said triglyceride of saturated C₈-C₁₈ fatty acids is dispersed in an amount of 1-3% by weight of the weight of the silicone elastomer.

10. The sheet according to claim 9, wherein said triglyceride of saturated C₈-C₁₈ fatty acids is selected from the group consisting of Caprylic/Capric Triglyceride, Caprylic/Capric/Stearic Triglyceride and Caprylic/Capric/Myristic/Stearic Triglyceride.

11. The sheet according to claim 9, wherein said triglyceride of saturated C₈-C₁₈ fatty acids is Caprylic/Capric Triglyceride.

12. The sheet according to claim 1, wherein said layer of silicone elastomer has a thickness of between 0.2 and 1.5 mm.

13. The sheet according to claim 1, wherein said silicone elastomer is a vinyl-substituted polysiloxane crosslinked with a polyalkyl hydrosiloxane.

14. The sheet according to claim 13, wherein said silicone elastomer is a Bis-Vinyl Dimethicone/Dimethicone Copolymer (INCI nomenclature).

15. A process for the production of a sheet for cutaneous application according to claim 1 comprising a support layer made of loosely woven fabric embedded in a layer of silicone elastomer incorporating vitamin E or an ester thereof, wherein said layer of silicone elastomer has a thickness less than or equal to 2.0 mm, said silicone elastomer contains an elasticity modifier consisting of a triglyceride of saturated C₈-C₁₈ fatty acids, and said silicone elastomer is a vinyl-substituted polysiloxane crosslinked with a polyalkyl-hydrosiloxane, which process comprises the steps of:

- a) dispersing at room temperature and while stirring the vitamin E or its ester and the triglyceride of saturated C₈-C₁₈ fatty acids in a vinyl-substituted polysiloxane, in an amount equal to 3.8-84.4% and 2.9-21.1% by weight of the vinyl-substituted polysiloxane,
- b) adding, again while stirring, a polyalkyl hydrosiloxane in a weight ratio with respect to the vinyl-substituted polysiloxane ranging from 0.9:1.0 to 1.1:1.0, obtaining a homogeneous dispersion;
- c) depositing on the support layer made of loosely woven fabric said homogeneous dispersion in a layer with a

thickness of 0.2-2.0 mm and leaving it at room temperature for a time sufficient to obtain the formation of the sheet.

16. The process according to claim 15, wherein said vinyl-substituted polysiloxane is Bis-Vinyl Dimethicone and said polyalkylhydrosiloxane is Hydrogen-Dimethicone (INCI nomenclature).

17. The process according to claim 15, wherein in said step a) vitamin E acetate is dispersed in said vinyl-substituted polysiloxane in an amount of between 7.5-45% by weight of the weight of the vinylsubstituted polysiloxane.

18. The process according to claim 15, wherein said support layer made of loosely woven fabric is a cotton gauze.

19. A method for treating the formation of keloids and abnormal wound healing processes and for the treatment of already formed keloids in a skin area of a subject, comprising the application of a the sheet according to claim 1 to said skin area.

20. A method for treating sunburn in a skin area of a subject, comprising the application of the sheet according to claim 1 to said skin area.

21. A method for relaxing and moisturizing a skin area of a subject, comprising the application of the sheet according to claim 1 to said skin area.

22. The process according to claim 15, wherein the weight ratio of polyalkyl hydrosiloxane to vinyl-substituted polysiloxane is 1:1.

23. The process according to claim 15, where the time sufficient to obtain the formation of the sheet is 2-12 hours.

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