

Brigard & Castro

Abogados

Apartado 3692

SUPERINDUSTRIA Y COMERCIO

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el Conn 3802200

el/Fax (57 1) 2827976

(57 1) 3802700

Dependencia: 2020 DIVISION DE NUEVAS CREACIONES

AS 84 010

E Mail brncas@brigardycastro.com.co

Señores

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

DIVISION DE NUEVAS CREACIONES

E S D

REF Expediente No 00 097 840 solicitud de Patente a nombre de
COLGATE – PALMOLIVE COMPANY

RAMIRO CASTRO DUQUE, vecino de Bogotá, portador de la tarjeta profesional No 1003 del Consejo Superior de la Judicatura, obrando como apoderado de la Sociedad COLGATE – PALMOLIVE COMPANY, según lo acredita el documento de poder protocolizado en la Secretaría General bajo el No 131, de acuerdo con el Artículo 44 de la Decisión 486 de la Comisión de la Comunidad andina, me permito solicitar que se examine si la invención contenida en la solicitud en referencia es patentable

De acuerdo con lo anterior, me permito anexar el recibo oficial de caja No 03-13,982 por valor de \$335 000

Señor Superintendente,



RAMIRO CASTRO DUQUE

C C No 170 322 de Bogotá

Código 340

T P No 1003 del C S J

Cra 7 No 16-56 Piso 9

Abril 07, 2003

CPB/hsr

NIT 800176089-2

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RECIBO OFICIAL DE CAJA 03 - 13,982
FECHA : FEBRERO 25 DE 2003

Industria y Comercio

SUPERINDUSTRIA Y COMERCIO

Radicacion : 80037040 0000003

Folios: 2 1 A

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Tramite : 002 PATENTES y 1 REGISTRO/ 538 PETICION
Dependencia 2020 DIVISION DE NUEVAS CREACIONES

***** CONSIGNACION *****

DEPOSITANTE	TIPO PAGO	BANCO	CUENTA	No PAGO	FECHA PAGO	Vr PAGO
BRIGARD & CASTRO LTDA	CONSIGNACION	BANCO POPULAR	050-00110-6	2199912	25/02/2003	14,370,000 00

***** CONCEPTO *****

CANT	RENTISTICO	CONCEPTO	TOTAL CONCEPTO
1	30005-01-01 SOLICITUDES	112 PTC CAP-1 EXAMEN DE PATENTIBILIDAD	335,000 00
		TOTAL	\$ 335,000 00

SON: TRESCIENTOS TREINTA Y CINCO MIL PESOS

RESPONSABLE :



RECIBO DE CAJA APLICADO AL EXPEDIENTE No

Carrera 13 No 27-00 Pisos 5 7 y 10
Commutador 382 0840
Fax 350 5220
E-mail info@sic.gov.co
www.sic.gov.co
Bogotá, D C Colombia

DIVISION DE NUEVAS CREACIONES

RADICACIÓN EXPEDIENTE No 00-07840

**EL EXTRACTO DE LA PRESENTE SOLICITUD DE PATENTE DE INVENCION
FUE PUBLICADO EN LA GACETA DE PROPIEDAD INDUSTRIAL No 525, DE
FECHA 28 DE FEBRERO DE 2003, EL TERMINO HABIL SEÑALADO POR LA
LEY EXPIRA EL 29 DE MAYO DE 2003**

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 calga 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 _____

United States Patent [19]

Finchetti

[11] Patent Number: 4,885,157

[45] Date of Patent: Dec. 5, 1989

[34] DERMAL COSMETIC COMPOSITION AND APPLICATIONS THEREFOR

[76] Inventor: Mary G. Finchetti, 12206 Cedar Gap Ln., Houston, Tex. 77072

[21] Appl. No. 14,382

[22] Filed: Feb. 12, 1987

[31] Int. Cl.⁴ _____ A61K 7/40; A61K 7/42; A61K 7/44; A61K 7/48

[32] U.S. Cl. _____ 434/88; 434/90; 434/92; 434/193.1; 514/773; 514/776; 514/783; 514/844; 514/847; 514/859; 514/860; 514/861; 514/863; 514/873; 514/886; 514/887; 514/904

[38] Field of Search _____ 514/783, 776, 844, 847, 514/886, 859, 860, 861, 863, 904; 434/39, 60

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Primary Examiner—Dale R. Orr

Attorney, Agent, or Firm—James L. Jackson & Assoc.

[57]

ABSTRACT

Provided is a cosmetic composition which beautifies and moisturizes the skin of a human being. The composition may also have therapeutic effects on the human skin such as the removal of lines or wrinkles, dissolution of fat pockets, the removal of bags under the eyes, and the closing of pores or gaps in the skin to render a smooth uniform appearance. The composition is comprised of seven basic ingredients, which include:

live yeast cells,
salicylic acid,
carotene,
RNA,
DNA,
water and
albumen.

These core ingredients generally make up from about 80% to 100% of the composition used in the treatment, and are the basis for the advantages realized thereby. Significant and long-lasting results are particularly achieved upon application of the composition to the human skin with exposure to sunlight.

16 Claims, No Drawings

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Methionine	.435 g.
Histidine	.672 g.
Leucine	1.974 g.
Lysine	2.178 g.
Cystine	1.62 g.

VITAMIN CONTAINING COMPOSITION

Folic acid	100 g.
Vitamin B ₁	.002 g.
Vitamin B ₂	.003 g.
Niacin	.018 g.
Vitamin B ₆	.030 g.
Vitamin B ₁₂	.0003 g.
Biotin	.03 g.
Pantothenic acid	1.3 g.
Choline	.230 g.
Inositol	150 g.
Para-aminobenzoic acid	.0015 g.

SUPPLEMENTAL COMPOSITION

San Pellan	430 g.
Essential Oil of Primrose	210 g.
Alma Veen	75 ml.

EXAMPLE 1

A composition was prepared using 8½ parts by weight by the basic composition, ½ part by weight of the amino acid containing composition, ½ part by weight of the vitamins containing composition and ½ part by weight of the supplemental composition. This composition was used in a treatment of an 80 year old female Caucasian, having a fair complexion. Prior to the treatment, the woman's face exhibited extreme sagging in the skin, the eyes were very much affected due to a depletion of skin elasticity and the natural aging process and could not be completely closed except when lying down. There were heavy, deep set lines around the eyes, mouth, forehead, neck and chin. The tone of the muscles and skin was also very bad.

Five treatments were administered within a period of four days. Each treatment was as that described in Example 1. A rapid change was noticed in the skin with the treatments. The skin around the eye area was completely reversed and the gap between the lower eye socket and the nose membrane was completely sealed together. Most of the lines disappeared, the skin became 75% firmer than before the treatment and much of the sagging was eliminated. The coloring of the skin was also much more even. Overall, the entire face took on a glow and had a much more youthful appearance.

EXAMPLE 2

A composition such as that prepared in Example 4 was applied to the skin of a 45 year old Caucasian female having a fair complexion, some freckles, and dry skin. The application of the composition was made to the face, chest, neck and breasts. Prior to the treatment, fatty pockets were evident under the eyes, deep set lines were apparent under and at the side of the eyes, the woman's coloring and texture was uneven and there was cracking of the lips at the borders of the mouth. As well, generally poor muscle and skin tone was apparent.

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The woman was treated for five consecutive days, one treatment each day. Each treatment consisted of 45 minutes to one hour, with the composition then being removed. The change in the complexion and skin was quite evident. The bags under the eyes and the sagging skin was completely reversed, with the fatty pockets under the eyes being gone. The treatment to the chest, neck and upper breasts produced the same results. The lines and gaps, as well as the cracks around the mouth, were not detectable and the texture of the skin was greatly improved.

EXAMPLE 3

A formulation comprising 8½ parts by weight of the basic composition, ½ part by weight of the amino acid containing composition, ½ part by weight of the vitamin containing composition and ½ part by weight of the supplemental composition was used in the treatment of an elderly lady having extensive sagging and wrinkling around the eyes. The treatments were as disclosed in Example 1, and occurred once a day for two weeks, with the exposure being to natural sunlight for a period of time of about 40 minutes each day. After the two week treatment, the majority of wrinkles and sagging around the eyes has been reversed.

EXAMPLE 4

In this example, a middle aged male of about 46 years was treated for extensive swelling of the lower eyelids and large pockets of fat and fluid buildup underneath the eyes. The patient had been on regular doses of cortisone. The formulation used comprised the basic composition ingredients, 9 parts by weight, and 1 part by weight of the supplemental composition, along with 2.1 milligrams of calcium, 60 milligrams of magnesium, 18 milligrams of niacin and 5.7 milligrams of copper. The formulation was applied once a day with the applied formulation being exposed to natural sunlight for a period of about 25 minutes. As the treatment progressed, the extensive swelling was reduced and the large pockets of fat and fluid buildup under the eyes were also noticeably reduced.

Thus, from the foregoing, it can be seen that by using the basic composition, either alone or in combination with the various other ingredients, very beneficial results, as well as therapeutic, results can be elicited with regard to problem skin disorders. In all of the Examples, an exposure to sunlight or artificial sunlight was employed. This has been found to be most beneficial. Without the exposure, however, the benefits would as well be achieved, but not nearly as fast, as significant or as long lasting.

Although the invention has been described with preferred embodiments, it is to be understood that variations and modifications may be resorted to as will be apparent to those skilled in the art. Such variations and modifications are to be considered within the purview and the scope of the claims appended hereto.

What is claimed is:

1. A beautifying and moisturizing composition for dermal application, which comprises cosmetic effective amounts of the following components in parts by weight:

Five yeast cells, minimum, maximum,	about 1 to about 8 parts about ½ to about 1 part about ¼ to about 1½ parts
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RNA, DNA, water and albumen,	about 2 to about 4 parts about 1 to about 3 parts about 2 to about 6 parts about $\frac{1}{2}$ to about $2\frac{1}{2}$ parts.
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2. The composition of claim 1, wherein the live yeast cells are saccharomyces cerevisial and the selenium is of a finely powdered form.

3. The composition of claim 1, wherein the composition comprises about 6 parts live yeast cells, about $\frac{1}{2}$ part selenium, about 1 part carotene, about 3 parts RNA, about 2 parts DNA, about 3 parts water and 1 part albumen.

4. The composition of claim 3, wherein the live yeast cells are saccharomyces cerevisial and the selenium is finely powdered.

5. The composition of claim 1, wherein the composition further comprises at least one of the following supplemental ingredients:

Alanine Arginine Aspartic acid Serine Threonine Tryptophane Tyrosine Valine Glutamic acid Glycine Isolucine Proline Phenylalanine Methionine Histidine Leucine Lysine Cysteine Copper Calcium	Folic acid Vitamin B ₁ Vitamin B ₂ Niacin Vitamin B ₆ Vitamin B ₁₂ Biotin Pantothenic acid Choline Inositol Para-aminic Benzoic acid Bee Pollen Evening Oil of Primrose Aloe Vera Vitamin K Chromium Vitamin E Vitamin C Magnesium
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6. The composition of claim 1, wherein the supplemental ingredients comprise from 5 to about 20 percent by weight of the entire composition.

7. The composition of claim 1, wherein the composition further comprises a combination of the following supplemental ingredients in an amount of less than about 20 percent by weight of the total composition.

Alanine Arginine Aspartic acid Serine Threonine Tryptophane Tyrosine Valine Glutamic acid	Glycine Isolucine Proline Phenylalanine Methionine Histidine Leucine Lysine Cysteine
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8. The composition of claim 1, wherein the composition further comprises a combination of the following supplemental ingredients in an amount of less than about 20 percent by weight of the total composition.

- Folic acid
- Vitamin B₁
- Vitamin B₂
- Niacin
- Vitamin B₆
- Vitamin B₁₂

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- Biotin
- Pantothenic Acid
- Choline
- ~~Inositol~~

Para-aminic Benzoic acid.

9. The composition of claim 1, wherein the composition further comprises a combination of the following supplemental ingredients in an amount of less than about 20 percent by weight of the total composition.

- Bee Pollen
- Evening Oil of Primrose
- Aloe Vera.

10. The composition of claim 1, wherein the composition comprises $8\frac{1}{2}$ parts by weight of a combination of the following components

- live yeast cells,
- selenium,
- carotene,
- RNA,
- DNA,
- water and
- albumen,

and further comprises $\frac{1}{2}$ part by weight of a combination of the following components

Alanine Arginine Aspartic acid Serine Threonine Tryptophane Tyrosine Valine Glutamic acid	Glycine Isolucine Proline Phenylalanine Methionine Histidine Leucine Lysine Cysteine
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$\frac{1}{2}$ part by weight of a combination of the following components:

- Folic acid
- Vitamin B₁
- Vitamin B₂
- Niacin
- Vitamin B₆
- Vitamin B₁₂
- Biotin
- Pantothenic acid
- Choline
- ~~Inositol~~

Para-aminic Benzoic acid

and $\frac{1}{2}$ part by weight of a combination of the following components:

- Bee Pollen
- Evening Oil of Primrose
- Aloe Vera.

11. A method for cosmetically treating the skin to thereby moisturize and beautify the skin which comprises applying the composition of claim 1 to the area of skin to be treated for a sufficient length of time to elicit its cosmetic beneficial results, removing the composition, and then repeating the application periodically

12. The method of claim 11, wherein the composition is exposed to natural or artificial sunlight subsequent to the application of the composition to the area of skin to be treated.

13. The method of claim 12, wherein the duration of the exposure is in the range of from about 15 minutes to about 60 minutes.

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14. The method of claim 12, wherein the duration of the exposure is in the range of from about 20 to 25 minutes.
15. The method of claim 12, wherein the composition is applied in several layers.
16. The method of claim 15, wherein the composition was applied in three layers,

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the first layer being applied as a thin layer which is massaged into the area of the skin to be treated, the second layer being applied so that the composition thinly covers the skin area to be treated, and the third layer being applied so that the composition provides a thick cover over the area of the skin to be treated.

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WELTORGANISATION FÜR GEISTIGES EIGENTUM
Internationales Büro
INTERNATIONALE ANMELDUNG VERÖFFENTLICHT NACH DEM VERTRAG ÜBER DIE
INTERNATIONALE ZUSAMMENARBEIT AUF DEM GEBIET DES PATENTWESENS (PCT)

(51) Internationale Patentklassifikation 6 A61K 7/06, 7/48	A1	(11) Internationale Veröffentlichungsnummer W 96/27363 (43) Internationales Veröffentlichungsdatum: 12. September 1996 (12.09.96)
(21) Internationales Aktenzeichen: PCT/EP96/00652 (22) Internationales Anmeldedatum: 15. Februar 1996 (15.02.96) (36) Prioritätsdaten: 195 07 905 1 7 März 1995 (07.03.95) DE (71) Anmelder (für alle Bestimmungsstaaten außer US): WELLA AKTIENGESELLSCHAFT [DE/DE]; Berliner Allee 65, D-64274 Darmstadt (DE). (72) Erfinder; und (73) Erfinder/A Anmelder (nur für US): BIDACZOK, Rudolf [DE/DE], Brüder-Grimm-Strasse 12, D-64342 Seckeln (DE), KONRAD, Eugen [DE/DE], Mecklenburger Strasse 101, D-64297 Darmstadt (DE). (74) Gemeinsamer Vertreter: WELLA AKTIENGESELLSCHAFT; Berliner Allee 65, D-64274 Darmstadt (DE).	(81) Bestimmungsstaaten: BR, JP, US europäisches Patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE). Veröffentlicht Mit internationalem Recherchenbericht. Vor Ablauf der für Änderungen der Ansprüche zugelassenen Frist. Veröffentlichung wird wiederholt falls Änderungen eintreffen.	
(54) Title: HAIR- AND SKIN-TREATMENT AGENT (54) Bezeichnung: HAAR- UND HAUTBEHANDLUNGSMITTEL (57) Abstract The invention concerns a cosmetic agent suitable for treatment of both the skin and the hair and containing a combination of a) 0.1 to 25 % by wt. of at least one salt of choline of an inorganic acid or an inorganic carboxylic acid or a polyacrylic acid homopolymer or copolymer; and b) 0.1 to 10 % by wt. of at least one physiologically compatible aliphatic organic acid. The agent proposed can be used as a hair-treatment agent, a skin-treatment agent or a hair- and skin-treatment agent. The agent improves the wet-combing characteristics of the hair, shows good compatibility with the scalp and gives the hair a soft feel and good shine. The agent proposed shows good compatibility with the skin and eyes, gives the hair a well groomed appearance and is also biodegradable. (57) Zusammenfassung Gegenstand der vorliegenden Erfindung ist ein kosmetisches Mittel, das sich sowohl zur Haut- als auch zur Haarbehandlung eignet, welches einen Gehalt an einer Kombination aus a) 0,1 bis 25 Gewichtsprozent mindestens eines Cholin Salzes einer anorganischen Säure oder einer organischen Carbonsäure oder eines Polyacrylsäurehomo- oder Copolymerisates und b) 0,1 bis 10 Gewichtsprozent mindestens einer physiologisch verträglichen aliphatischen organischen Säure enthält. Das erfindungsgemäße Mittel kann als Haarbehandlungsmittel, als Hautbehandlungsmittel und als Haar- und Hautbehandlungsmittel vorliegen. Das Mittel verbessert die Naßkammbarkeit der Haare, weist eine gute Kopfhautverträglichkeit auf und verleiht dem Haar einen angenehmen Griff und einen schönen Glanz. Das erfindungsgemäße Mittel weist eine gute Haut- und Augenverträglichkeit auf, verleiht der Haut ein gepflegtes Aussehen und ist zudem gut biologisch abbaubar.		

Beispiel 7: Körperlotion Öl-in-Wasser

10,0	g	Cetylstearyl-octanoat
3,0	g	Sorbitanstearat
3,0	g	Polyoxyethylen (20) sorbitanmonolaurat
4,0	g	Cetylstearylalkohol
1,0	g	Dimethylpolysiloxan
0,1	g	Methylparaben
0,4	g	<u>Cholinpolyacrylat</u>
5,0	g	Glycerin
0,3	g	<u>Cholin-zitrat</u>
0,5	g	Milchsäure
<u>72,7</u>	g	Wasser, enthärtet
100,0	g	

Die Körperlotion gemäß Beispiel 7 läßt sich auf der Haut gut verteilen, zieht rasch ein, erhöht die Hautfeuchtigkeit und hinterläßt ein angenehmes Gefühl

Sämtliche in der Anmeldung angegebenen Prozentzahlen stellen Gewichtsprozentage dar

Patentansprüche

- 1 Wasserhaltiges kosmetisches Mittel, enthaltend eine Kombination aus
 - a) 0,1 bis 25 Gewichtsprozent mindestens eines Cholinsalzes einer anorganischen Säure oder einer organischen Carbonsäure oder Polyacrylsäurehomo- oder Copolymerisates und
 - b) 0,1 bis 10 Gewichtsprozent mindestens einer physiologisch verträglichen aliphatischen organischen Säure
- 2 Kosmetisches Mittel nach Anspruch 1, dadurch gekennzeichnet, daß es 3 bis 15 Gewichtsprozent des Cholinsalzes enthält
- 3 Kosmetisches Mittel nach einem der Ansprüche 1 oder 2, dadurch gekennzeichnet, daß es als Cholinsalz, Cholinziträt, Cholintartrat, Cholinchlorid oder Cholinpolyacrylat enthält
- 4 Kosmetisches Mittel nach einem der Ansprüche 1 bis 3, dadurch gekennzeichnet, daß es 0,1 bis 5 Gewichtsprozent der physiologisch verträglich aliphatisch organischen Säure enthält



US005571518A

United States Patent [19][11] **Patent Number** 5,571,518

Pillai et al.

[45] **Date of Patent** Nov 5, 1996[54] **COSMETIC COMPOSITIONS CONTAINING TRICHOLINE CITRATE**5,376,646 12/1994 Pittrof et al. 514/78
5,391,350 2/1995 Carriglio et al. 574/23[75] **Inventors:** Suresh Kumar Pillai, Wyne; Mandisha N Mahajan, Edgewater Anthony V. Rawlings, Wyckoff all of N.J.[73] **Assignee:** Chesebrough-Pond's USA Co., Division of Cosceps, Inc., Greenwich, Conn.[21] **Appl. No.** 546,959[22] **Filed** Oct. 30, 1995[31] **Int. Cl.⁶** A61K 7/42, A61K 7/06; A61K 7/48[52] **U.S. Cl.** 424/481 424/39, 424/70.1[58] **Field of Search** 424/401 59 70.1[56] **References Cited****U.S. PATENT DOCUMENTS**

2,865,938	12/1958	Rosenfelder	260/439
3,393,229	7/1968	Felgh et al.	424/293
4,275,059	6/1981	Pizza et al.	424/204
4,816,568	3/1989	Hamilton et al.	530/399
5,166,139	11/1992	Bombardelli et al.	514/26
5,244,665	9/1993	Natraj et al.	424/401

OTHER PUBLICATIONSvan Scott et al., "Control of Keratinization with α -Hydroxy Acids and Related Compounds", *Arch. Dermatol.*, vol. 110, Oct. 1974, pp. 586-590.Bazzardesa et al., "AHA Mechanisms of Action" *Cosmetics & Toiletries*, vol. 110, Jun. 1995, pp. 30-31

Abstract of DE 4 310 015

Abstract of JP 6179613

Abstract of SU 1811403

Abstract of EP 0 479 121

Primary Examiner—John C. Blanton**Assistant Examiner**—Margaret Glass**Attorney, Agent, or Firm**—Rimma Mitalman[57] **ABSTRACT**

Cosmetic compositions containing tricholine citrate (TCC). TCC stimulates keratinocyte growth, does not inhibit keratinocyte differentiation and increases the phospholipid levels in keratinocytes. Thus, TCC provides improved conditioning, improved youthful appearance, moisturization and improvement in the appearance of photodamaged skin.

4 Claims, No Drawings

COSMETIC COMPOSITIONS CONTAINING TRICHOLINE CITRATE

FIELD OF THE INVENTION

The invention relates to a composition suitable for topical application to human skin for the treatment and conditioning of the skin and for reducing the damaging effects of UV light on human skin, containing an effective amount of tricholine citrate.

BACKGROUND OF THE INVENTION

Tricholine citrate (hereinafter "TCC") is an ester of citric acid with three choline molecules.

Citric acid is a hydroxy tricarboxylic acid. Since the discovery by van Scott et al., "Control of Keratinization with α -Hydroxy Acids and Related Compounds", *Arch. Dermatol.*, Vol. 110, October 1974, pp. 586-590, that hydroxyacids are effective for the treatment of hyperkeratotic disorders of the skin, several hydroxy acids and related compounds have been used extensively in dermatologic and cosmetic preparations. The reported cosmetic properties of hydroxy acids include improved skin texture, improved skin brightness and firmness, decreased wrinkling and decreased pigmentation. See e.g. Bernardeca et al., "AHA Mechanisms of Action", *Cosmetics & Toiletries*, Vol. 110, June 1995, pp. 30-31.

Triesters of citric acid with alkyl or aryl groups have been claimed to have anti-aging and UV protecting effects. See e.g., Natraj et al., U.S. Pat. No. 5,244,665. Triethyl and tributyl esters of citric acid have been shown to be effective in the treatment of photodamaged and/or hyperpigmented skin, and in slowing down the aging process, in addition to the photoprotective action. The use of TCC, however, has not been taught or suggested for use in skin treatment compositions. Natraj et al. do not appear to teach or suggest either TCC or any nitrogen or amine-containing citrate esters.

Choline is an essential nutrient for phospholipid, sphingolipid and sphingomyelin biosynthesis in all cells. In addition, choline acts as a methyl donor for carnitine biosynthesis which is required for normal fatty acid turnover. Choline deficiency results in reduced lipoprotein biosynthesis, decreased membrane turnover and increased triglyceride accumulation. Choline deficiency in the epidermis could result in lower barrier lipid formation leading to an abnormal water barrier and poor skin condition. Choline in the form of phosphatidyl choline or phosphoryl choline and their derivatives have been used in cosmetic compositions and have been claimed to have multiple beneficial effects on skin, such as anti fungal effects, wound healing enhancers, dry skin benefits, improving transepidermal water loss, moisturizing effects, anti-acne effects, UV protecting effects, conditioning benefits, humectant effects, and anti-inflammatory effects. See U.S. Pat. No. 5,391,550, U.S. Pat. No. 5,376,646; Abstract of German Patent Application No. 4 310 015, Abstract of Japanese Patent Specification No. 6179613, Abstract of Soviet Union Patent Specification No. 1811403, Abstract of European Patent Application No. 0 479 121, U.S. Pat. No. 5,166,139. Patented compounds include phosphatidyl choline, phosphoryl choline, acylated choline, sphingomyelin or their derivatives.

Choline salicylate has been employed as an anti-inflammatory and analgesic agent for topical use. See U.S. Pat. No. 4,275,059 (Flora et al.)

TCC is a common inexpensive chemical used in the past as an effective iron chelator. See Rosenfelder, U.S. Pat. No. 2,865,938. TCC has been used to stabilize animal growth hormone preparations (see Hamilton et al., U.S. Pat. No. 4,816,568) and to treat iron deficiency anemia (see Feigh et al., U.S. Pat. No. 3,395,229). No toxicity or adverse effects have been associated with this molecule since its individual components, citric acid and choline, are naturally occurring metabolites in cells.

Skin treatment or cosmetic compositions containing tricholine citrate have not been disclosed. None of the art described above teaches the use of TCC for the growth of skin cells or skin cell cultures. Furthermore, the art does not appear to teach or suggest the use in cosmetic compositions of any citrate ester wherein citric acid is esterified with any compound which serves as an essential nutrient for skin cells.

The top layer of human skin or the epidermis is composed of many different cell types including keratinocytes, melanocytes and langerhans cells. Keratinocytes are the major cell type of the epidermis (75-80% of the total number of cells in the human epidermis). Within the epidermis the keratinocytes reside in four distinct stages of differentiation. The basal layer rests on the basal lamina separating epidermis from the dermis. These cells are large columnar rapidly proliferating cells. These basal cells migrate upward within the epidermis, initiated by the process of differentiation. The layer above the basal cells is the spinous layer. The cells in the spinous layer initiate the production of proteins characteristic of the differentiated epidermis. The granular layer lying above the spinous layer, is characterized by electron-dense granules. This layer is responsible for the synthesis of lipid molecules required for the formation of the water impermeable barrier of the skin. The topmost layer of the skin, the stratum corneum, is formed from the granular layer by the destruction of cellular organelles. The cells in the stratum corneum, corneocytes, contain extensively cross-linked proteins, surrounded by a highly resistant cell envelope. The corneocytes are embedded in a bed of specific lipid structures (analogous to bricks on a bed of mortar) and this structure provides the protective barrier for the skin. The outermost layer of corneocytes is peeled off from the skin during the normal process of desquamation. Differentiation of the epidermal keratinocytes is the driving force for the normal desquamation process to occur. Epidermal differentiation is important for providing the essential function of the skin, namely to provide a protective barrier against the outside environment and to prevent loss of water from the body. The rate of synthesis of DNA, determined by the incorporation of radiolabeled substrate [3 H]thymidine, is an indicator of keratinocyte proliferation. An increase in cornified envelopes and the enzyme transglutaminase, which is responsible for the formation of cornified envelopes, indicates an increase in keratinocyte differentiation. The basal cells which have the highest rate of growth, are the least differentiated. The most differentiated cells of the stratum corneum do not have the ability to proliferate. The increased proliferation of the basal cells is the driving force for the differentiation of the upper layer cells to form corneocytes.

The present invention is based, in part, on the discovery that TCC induces cell proliferation and increases cellular lipid levels in skin, both of which in turn result in increased benefits to skin, such as improved conditioning, improved youthful appearance, decrease in wrinkle appearance, moisturizing, and improvement in the appearance of photodamaged skin.

Accordingly, it is an object of the present invention to provide compositions for the treatment of skin using TCC as the active ingredient.

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It is another object of the invention to provide a method for treating the appearance of wrinkled, flaky, aged, or photodamaged skin and for promoting youthful appearance.

These and other objects of the invention will become more apparent from the detailed description and examples which follow

SUMMARY OF THE INVENTION

The invention provides a composition suitable for topical application to human skin, the composition containing as an essential ingredient, from 0.0001 to 50 wt. % of tricholine citrate and a cosmetically acceptable vehicle for tricholine citrate.

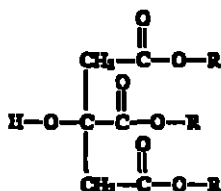
The vehicle enables tricholine citrate (TCC) to be dispersed onto the skin and distributed therein. According to the invention, TCC is employed to increase keratinocyte proliferation and to increase phospholipid levels in keratinocytes, in order to improve skin appearance

The present invention also includes a method of improving or preventing the appearance of wrinkled, dry, flaky, aged, photodamaged skin and treating skin disorders (e.g., acne or psoriasis), which method includes applying to the skin a composition containing TCC.

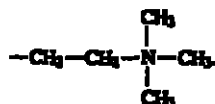
Compositions of the invention are intended for topical application to mammalian skin which is already in dry, flaky, wrinkled, aged, photodamaged condition or which suffers from a skin disorder, or, in the alternative, the inventive compositions may be applied prophylactically to normal healthy skin to prevent or reduce the deteriorative changes.

DESCRIPTION OF THE PREFERRED EMBODIMENT

Tricholine citrate is an essential ingredient of the inventive compositions. Tricholine citrate has the following structure:



where R represents a choline molecule having the structure



In general the amount of TCC in the inventive compositions is in the range of from about 0.0001% to about 50% by weight of the composition. Preferably, in order to lower cost and maximize the effect, the amount of TCC is in the range of from about 0.01% to about 10%, most preferably in the range of from 0.1% to 5%

COSMETICALLY ACCEPTABLE VEHICLE

The composition according to the invention also comprises a cosmetically acceptable vehicle to act as a dilutant, dispersant or carrier for the TCC in the composition, so as to facilitate its distribution when the composition is applied to the skin

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Vehicles other than water can include liquid or solid emollients, solvents, humectants, thickeners and powders. An especially preferred nonaqueous carrier is a polydimethyl siloxane and/or a polydimethyl phenyl siloxane. Silicones of this invention may be those with viscosities ranging anywhere from about 10 to 10,000,000 centistokes at 25° C. Especially desirable are mixtures of low and high viscosity silicones. These silicones are available from the General Electric Company under trademarks Viscell, SE and SF and from the Dow Corning Company under the 200 and 550 Series. Amounts of silicones which can be utilized in the compositions of this invention range anywhere from 5% to 95%, preferably from 25% to 90% by weight of the composition.

The cosmetically acceptable vehicle will usually form from 5% to 99.9%, preferably from 25% to 80% by weight of the emulsion, and can, in the absence of other cosmetic adjuncts, form the balance of the composition.

OPTIONAL SKIN BENEFIT MATERIALS AND COSMETIC ADJUNCTS

An oil or oily material may be present, together with an emulsifier to provide either a water-in-oil emulsion or an oil-in-water emulsion, depending largely on the average hydrophilic-lipophilic balance (HLB) of the emulsifier employed.

In a preferred embodiment of the invention, the inventive compositions further include at least one of the following ingredients which are particularly effective in combination with TCC.

Ceramides and/or other sphingolipids may be included in the inventive composition. Suitable ceramides and synthetic analogues thereof are disclosed in European Patent Application 534 286, European Patent Application 227 994, U.S. Pat. No. 5,175,321, U.S. Pat. No. 4,985,547, U.S. Pat. No. 5,028,416, U.S. Pat. No. 5,071,971, Japanese Patent Application No. 63192703, U.S. Pat. No. 4,468,519 and U.S. Pat. No. 4,950,688, all of which are incorporated by reference herein. Sphingolipids, including ceramides or their synthetic analogues, may be present in the inventive compositions at a level of from about 0.00001 to about 5%, preferably from about 0.00001 to about 1%, optimally from about 0.01 to 0.5%

Hydroxyacids are preferably included in the inventive compositions to enhance proliferation and to increase ceramide biosynthesis in keratinocytes, increase epidermal thickness, and increase desquamation of normal skin resulting in smoother, younger looking skin.

The hydroxy acid can be chosen from α -hydroxy acids β -hydroxyacids, other hydroxycarboxylic acids (e.g. dihydroxycarboxylic acid, hydroxy-dicarboxylic, hydroxytricarboxylic) and mixtures thereof or combination of their stereoisomers (DL, D or L)

Preferably the hydroxy acid (H) is chosen from α -hydroxy acids having the general structure:



where M is H— or $\text{CH}_2(\text{C}_2\text{H}_5)_f$ —,

f is an integer of from 1 to 27

g is an integer of from 2 to 54, and

h is 0 or 1

using chloroform:methanol (1:1). The chloroform phase was separated, dried under nitrogen, and resuspended in 200 μ l of chloroform for separation of the different lipid classes by column chromatography.

Aminopropyl columns (Waters division of Millipore) were washed with 3 mL of chloroform:isopropanol (2:1) followed by 2 mL of hexane to condition the column. The lipid samples were applied onto the column and the different lipid classes were separated using the following solvent systems: 2 mL of hexane:ethyl acetate (85:15) to elute the non-polar lipids (cholesterol and cholesterol esters), and 2 mL of chloroform:isopropanol (2:1) to elute the neutral lipids (ceramides, cerebroside, and monoglycerides) and 2 mL of 2% acetic acid in methanol to extract polar lipids (phospholipids and fatty acids).

Total cholesterol was quantitated using the cholesterol assay kit obtained from Sigma. Phospholipid quantitation in the neutral and polar lipid fractions were carried out by spotting the lipids onto High Performance Thin Layer Chromatography (HPTLC) silica gel plates and running in chloroform:methanol:acetic acid (47.5:2.25:0.25). Quantitation was performed by measuring the HPTLC plates in a solution containing 10% Copper Sulfate and 8% Phosphoric acid and

counts are present only in the phospholipid fraction, the amount of ^3H choline incorporated into the different lipid fractions were quantitated by running TLC of the fractions in the above solvent system, and the amount of radioactivity in the phospholipid fraction (origin) was quantitated using BioScan plate reader. The cpm of ^3H choline was plotted against the amount of cold choline or TCC added in the medium to assess the competition between choline supplied from TCC with ^3H choline.

EXAMPLE 1

Effect of Citrate Esters on Keratinocyte Proliferation

Effects of 24 hours exposure to 0.1 μM to 10 mM of citric acid, choline or the different citrate esters on keratinocyte DNA synthesis are shown in table 1. Rate of DNA synthesis calculated as cpm ^3H thymidine incorporated into cellular DNA/ μg of cell protein is expressed as % of control (no addition controls) $\pm$ SD. The actual amount of cpm/ μg protein of the control is 1103 $\pm$ 88.

TABLE 1

(μM)	Citric acid	Choline	TCC	TBC	TBC
0	100 $\pm$ 7.9	100 $\pm$ 7.9	100 $\pm$ 7.9	100 $\pm$ 7.9	100 $\pm$ 7.9
0.1	88.4 $\pm$ 15.5	125 $\pm$ 17.6	92.4 $\pm$ 6.8	112 $\pm$ 21.9	106 $\pm$ 8.4
1.0	74.5 $\pm$ 32.2	113 $\pm$ 12.0	97.7 $\pm$ 25.6	112 $\pm$ 13.1	100.0 $\pm$ 28
10	89.9 $\pm$ 20.3	109 $\pm$ 3.3	91.0 $\pm$ 14.0	79.1 $\pm$ 13.9	62.2 $\pm$ 19
100	88.7 $\pm$ 3.1	114 $\pm$ 12.0	94.5 $\pm$ 13.4	9.8 $\pm$ 2.3*	8.7 $\pm$ 3.5*
1000	63.9 $\pm$ 11.8	115 $\pm$ 24.0	102 $\pm$ 12.3	11.2 $\pm$ 9.2*	1.95 $\pm$ 1*
10,000	4.25 $\pm$ 2.2*	127 $\pm$ 10.7	19.7 $\pm$ 9.8*	1.2 $\pm$ 0.02*	0.305 $\pm$ 0*

*statistically significant compared to controls.
*triethylcitrate
*triethylcitrate

charring at 165 $^{\circ}$ C. for 15 minutes. Micrograms of phospholipids remaining at the origin in the extract were determined by reflectance densitometry and comparison with phospholipid standards.

ANALYSIS OF ^3H CHOLINE INCORPORATION INTO PHOSPHOLIPIDS OF KERATINOCYTES

Choline acts as an essential nutrient for the cellular phospholipid biosynthesis of keratinocytes. Choline present in the medium is used up by the cells for phospholipid biosynthesis. If TCC provides choline for the cells it will compete with the choline in the medium for incorporation into cellular phospholipids. When cells are incubated with ^3H -labelled choline, its incorporation into phospholipids will be decreased by the presence of unlabelled choline or TCC in the medium. Thus, a decrease in the ^3H choline incorporation into phospholipids indicates that TCC provides choline for keratinocyte lipid biosynthesis.

Keratinocytes grown to 80% confluence was treated with the different agents (choline, citrate, TBC, TBC or TCC) and labelled with 1 $\mu\text{Ci}/\text{ml}$ media of ^3H labelled choline (obtained from Amersham) for 24 hours. The wells were washed, total lipids were extracted using Bligh Dyer method as described above and the total counts in the chloroform phase was determined. To ascertain that the

The results indicate that all agents, except choline, at 10 mM levels inhibited DNA synthesis of keratinocytes. Both TBC and TBC were inhibitory above 10 μM . TCC had no growth inhibitory effects up to 1 mM. This study indicates that TCC is tolerated better than other citrate esters by keratinocytes in vitro, perhaps due to the choline present in the TCC. Choline even at 10 mM levels was in fact slightly growth stimulatory, in contrast to all the other agents tested. TBC and TBC were inhibitory at lower concentrations than citric acid and at or above 1 mM levels the cells showed signs of cytotoxicity in the presence of TBC or TBC.

The aged epidermis may be choline deficient due to the decreased capillary circulation to the skin. To simulate the choline-deficient in vitro system, keratinocytes were plated in complete medium and 48 hours later switched to choline-free medium. The cells were then grown for five days in the choline-free medium with or without addition of different amounts of choline or TCC. To determine whether TCC can provide choline for keratinocyte proliferation under these conditions, on day 5, the amount of ^3H thymidine incorporation into DNA was determined as in the previous experiment. The protein content of the wells were also quantitated. Both these parameters were expressed as % of control $\pm$ SD. The actual amount of DNA synthesis and protein content for the controls were 14584 $\pm$ 1737 cpm/ μg protein and 21 $\pm$ 4 μg protein/well respectively.

TABLE 2

(μ M)	DNA (Choline)	DNA (TCC)	Protein (Choline)	Protein (TCC)
0	100 $\pm$ 11.9	100 $\pm$ 6.3	100 $\pm$ 21.6	100 $\pm$ 18.6
1	261 $\pm$ 5.6*	345 $\pm$ 15.3*	197 $\pm$ 21.8*	233 $\pm$ 18.3*
10	313 $\pm$ 11.4*	319 $\pm$ 38.4*	264 $\pm$ 90*	229 $\pm$ 37*
100	315 $\pm$ 28.3*	332 $\pm$ 34.3*	276 $\pm$ 53*	215 $\pm$ 18*
1000	297 $\pm$ 11.3*	187 $\pm$ 33.0*	229 $\pm$ 29*	120 $\pm$ 29*
10,000	270 $\pm$ 11.3*	13.8 $\pm$ 0.9*	209 $\pm$ 13.7*	23 $\pm$ 1.5*

*statistically significant compared to control.

It can be seen from Table 2 that both choline and TCC increased the proliferation of keratinocytes (both DNA synthesis and protein content) at all TCC concentrations as 1 μ M. Only the highest concentration of TCC (10 mM) inhibited DNA synthesis, all other concentrations of TCC stimulated keratinocyte growth significantly in a choline-free medium. This indicates that choline from TCC becomes available to the cells for the synthesis of essential phospholipids required for the cell membrane synthesis.

EXAMPLE 2

Effects of Citrate Esters on Keratinocyte Differentiation

Proper skin conditioning requires enhanced proliferation and differentiation of epidermal keratinocytes. The different citrate esters were tested on their effect on cornified envelope (CE) formation, a marker of terminal differentiation of keratinocytes. Citrate esters were tested at 1 mM levels in medium containing 0.15 mM Ca. Levels are expressed as % of control $\pm$ SD. The CE formation for the control was 54.48 $\pm$ 31.8 cpm/ μ g cell protein.

TABLE 3

Agents	Choline	Citric acid	TCC	TBC	TBC
CE Levels (% Control)	135 $\pm$ 23.6	13.7 $\pm$ 1.1*	91.3 $\pm$ 54.0	23.6 $\pm$ 2.1*	18.6 $\pm$ 4.2*

*statistically significant effects

The data in Table 3 clearly indicates that choline increased cornified envelope formation whereas TCC had no effect. However, citric acid and other citrate esters all inhibited cornified envelope formation significantly. Thus, this data show that TCC is clearly superior to citric acid or other citrate esters in its effect on keratinocyte differentiation, i.e., TCC does not inhibit keratinocyte differentiation whereas other citrate esters do. As seen in Example 1 for the proliferation, choline content of TCC may protect it from the differentiation inhibitory effects of citric acid, whereas the other esters of citric acid are not protected.

Cornified envelope formation is determined by the activity of transglutaminase enzyme which cross-links all the envelope precursor proteins to form the envelope. This enzyme is calcium dependent and is inhibited by calcium chelators such as citric acid and citric acid esters. However, cornified envelope formation was not affected by TCC. To understand the reason for this, we determined the effect of different citrate esters on transglutaminase I levels in keratinocytes after 48 hour treatment with different amounts of the agents.

TABLE 4

(μ M)	Choline	TCC	TBC	TBC
0	100 $\pm$ 15	100 $\pm$ 15	100 $\pm$ 15	100 $\pm$ 15
1	121.8 $\pm$ 18	98.2 $\pm$ 4.5	100 $\pm$ 13	77.3 $\pm$ 10.7
10	124.3 $\pm$ 8.7*	94.5 $\pm$ 17	79 $\pm$ 13	76.7 $\pm$ 20.8
100	120.4 $\pm$ 11.3*	89.5 $\pm$ 14.2	79 $\pm$ 13	67.2 $\pm$ 11.9*

*statistically significant effects compared to controls.

As seen in Table 4, choline stimulated transglutaminase while TBC and TBC inhibited the enzyme. TCC had no significant effect on this enzyme. Therefore, it appears that the negative effect of citrate on transglutaminase is counteracted by the stimulatory effect of choline of TCC. This may be the reason for the neutral effect of TCC on keratinocyte differentiation while both TBC and TBC inhibited differentiation. Thus, TCC increases proliferation and does not inhibit differentiation of keratinocytes whereas citric acid and other citrate esters inhibit both proliferation and differentiation of keratinocytes. Furthermore, choline, a nutrient component of TCC, enhances differentiation, sug-

gesting TCC is clearly superior to other citrate esters for keratinocyte proliferation and differentiation.

EXAMPLE 3

Effect of Citrate Esters on Keratinocyte Lipid Synthesis

To demonstrate directly that choline from TCC is incorporated into phospholipids of keratinocytes, cells were labelled with 1 μ Cl 3 H choline/ml medium for 48 hours in the presence of different concentrations of the different citrate esters, citric acid or choline. The amount of 3 H choline incorporated into cellular phospholipids was determined and expressed as % of controls. The amount of 3 H choline incorporated into phospholipid fraction in the control was 252 $\pm$ cpm/ μ g protein.

TABLE 5

(μ M)	Citric acid	Choline	TCC	TBC	TBC
0	100 $\pm$ 16.5	100 $\pm$ 16.5	100 $\pm$ 16.5	100 $\pm$ 16.5	100 $\pm$ 16.5
10	91.4 $\pm$ 12.7	61.6 $\pm$ 7.8*	67.9 $\pm$ 8.9*	81.1 $\pm$ 7.0	114 $\pm$ 8.9
100	77.5 $\pm$ 19.5	36.9 $\pm$ 1.6*	20.8 $\pm$ 0.3*	120.7 $\pm$ 6.7	89.3 $\pm$ 1.9
1000	74.1 $\pm$ 28.8	10.8 $\pm$ 5.5*	4.5 $\pm$ 1.9*	81.1 $\pm$ 12.0	82.8 $\pm$ 22

*statistically significant effects compared to controls.

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The data indicate that both choline and TCC compete with ^3H choline for incorporation into cellular phospholipids. Choline competition is expected since it is competing with the same molecule (the only difference is in the ^3H label) for incorporation. The fact that TCC acts similar to choline is a direct demonstration that choline from TCC becomes available to cells for cellular phospholipid synthesis. Other esters of citric acid and citrate itself have no significant effect on choline incorporation into phospholipid fraction.

To determine whether TCC treated cells have higher levels of lipids the following experiment shown in Table 6 was conducted. Keratinocytes were treated with different concentrations of TCC for 48 hours and the lipid levels of the cells were quantified. The amounts of cholesterol, fatty acids and phospholipids were quantified and expressed as % of control. Amount of cholesterol was 7.34 $\pm$ 0.14, fatty acid was 21.4 $\pm$ 2.5 and phospholipid was 5.8 $\pm$ 1.26 ng/ μ g cell protein.

TABLE 6

Cholesterol, fatty acid and phospholipid levels of keratinocytes treated with TCC			
(μ M)	Cholesterol	Fatty acids	Phospholipids
0	100 $\pm$ 1.85	100 $\pm$ 12.2	100 $\pm$ 21.7
1	83.3 $\pm$ 10.2	96.9 $\pm$ 8.2	77.1 $\pm$ 9.3
10	111.3 $\pm$ 24.1	83.9 $\pm$ 6.8	112.4 $\pm$ 24.4
100	78.3 $\pm$ 21.7	78.1 $\pm$ 12.4	148.2 $\pm$ 26.9*
1000	69.3 $\pm$ 3.7*	76.7 $\pm$ 16.7	187.3 $\pm$ 9.3

*statistically significant effects compared to controls.

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95

100

EXAMPLE 4

This example illustrates a high internal phase water-in-oil emulsion incorporating the inventive composition.

	% w/w
TCC	0.5
1,3-bis(4-hydroxyphenyl)-2-isobutylidenebutane	0.2
Brij 92*	5
Butane-2,3	0.5
MgSO ₄ ·7H ₂ O	0.5
Butylated hydroxy toluene	0.01
Perfume	qs
Water	to 100

*Brij 92 is polyoxyethylene (2) octyl ether

EXAMPLE 5

This example illustrates an oil-in-water cream incorporating the inventive composition.

	% w/w
TCC	2
Isobutyl oil	4
1,3-bis(4-hydroxyphenyl)-2-isobutylidenebutane	1
Brij 56*	4
Alcol 16RD*	4
Trichloroethylene	0.75
Butane-1,3-diol	5
Xanthan gum	0.5
Perfume	qs
Butylated hydroxy toluene	0.01
Water	to 100

*Brij 56 is octyl alcohol POE (10)
Alcol 16RD is octyl alcohol

EXAMPLE 6

This example illustrates an alcoholic lotion incorporating the composition according to the invention.

	% w/w
TCC	5
1,3-bis(4-hydroxyphenyl)-2-isobutylidenebutane	0.1
Ethanol	40
Perfume	qs
Butylated hydroxy toluene	0.01
Water	to 100

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EXAMPLE 7

This example illustrates another alcoholic lotion containing the inventive composition

	% w/w
TCC	10
1,3-dimethyl-2-imidazolidinone	0.01
Ethanol	40
Ascorbic acid	0.1
Perfume	qs
Water	to 100

EXAMPLE 8

This example illustrates a moisture cream incorporating the composition of the invention.

	% w/w
TCC	2
1,3-dimethyl-2-imidazolidinone	0.2
Silicone oil 200 cSt	7.5
Glycerolmonostearate	3
Crotonyl alcohol	1.6
Polyacrylate-(20)-ethyl alcohol	1.4
Xanthan gum	0.3
Paral 1789	1.3
Octyl methacrylate (PAROL MCO)	7
Perfume	qs
Color	qs
Water	to 100

EXAMPLE 9

This example illustrates a non-aqueous skin care composition incorporating the inventive combination.

	% w/w
TCC	5
1,3-dimethyl-2-imidazolidinone	1
Silicone gum SR-90 ¹	10
Silicone fluid 343 ²	20
Silicone fluid 344 ³	50.39
Squalene	10
Linoleic acid	0.01

16
-continued

	% w/w
Cholesterol	0.03
2-hydroxy- α -octoic acid	0.7
Vitamin E tocopherol	0.5
Retinol oil	0.5
Ethanol	2

¹A dimethyl siloxane polymer having a molecular weight of at least 30,000 and a viscosity of at least 10,000 centistokes at 25° C., available from GEC

²Dimethyl siloxane cyclic polymer, available from Dow Corning Corp.

³Dimethyl siloxane linear, available from Dow Corning Corp.

It should be understood that the specific forms of the invention herein illustrated and described are intended to be representative only. Changes, including but not limited to those suggested in this specification, may be made in the illustrated embodiments without departing from the clear teachings of the disclosure. Accordingly, reference should be made to the following appended claims in determining the full scope of the invention

What is claimed is:

1. A method of enhancing keratinocyte proliferation in skin, the method comprising applying to the skin composition comprising from 0.0001 to 50 wt. % by weight of the composition of tricholine citrate and a cosmetically acceptable vehicle.

2. A method for treating the appearance of wrinkled, dry, flaky, aged, or photoaged skin comprising applying to the skin a composition comprising from 0.0001 to 50 wt. % by weight of the composition of tricholine citrate and a cosmetically acceptable vehicle.

3. A method of enhancing phospholipid levels in skin keratinocytes, the method comprising applying to the skin a composition comprising from 0.0001 to 50 wt. % by weight of the composition of tricholine citrate and a cosmetically acceptable vehicle.

4. A topical composition comprising from 0.0001 to 50 wt. % by weight of the composition of tricholine citrate, a cosmetically acceptable vehicle, and an additional cosmetic ingredient selected from the group consisting of an alpha hydroxy acid, a sunscreen, a tanning agent, a skin anti-wrinkling agent, an anti-dandruff agent, an anti-acne agent, a hair growth stimulant and a perfume.

* * * * *

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HH

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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

DIVISION DE NUEVAS CREACIONES

2020

Bogotá, D C , Agosto 10 de 2008

Abogado

RAMIRO CASTRO DUQUE

ASUNTO

Radicación No

00 097 840

Trámite

002

Evento

001

Actuación

430

Oficio No

00009404

Folios

0

Como resultado del examen de patentabilidad de la solicitud de patente de invención, realizado según lo establece el artículo 45 de la Decisión 486 de la Comisión de la Comunidad Andina, se notifica el siguiente concepto técnico

Título de la solicitud "Composición Humectante"

1 Documentos estudiados

Para el presente estudio se tuvieron en cuenta el capítulo descriptivo comprendido en los folios 6 - 25 y el capítulo reivindicatorio de los folios 26 - 28 de la solicitud

2 Objeto de la invención

El objeto de la presente solicitud de patente de invención consiste en

Las reivindicaciones 1 - 18 se refieren a una composición que contiene (a) humectante de estructura $(CH_3)(CH_3)(CH_3)N^+(CH_2)X$ en donde X es CH_2OH , $CHOHCH_2CO_2^-$ ó sus mezclas y (b) un vehículo compatible con la piel. Opcionalmente es un líquido, sólido, crema, loción ó gel, contiene ácido orgánico, tensioactivos, agente oclusivo

Las reivindicaciones 19 - 21 se refieren al proceso para aumentar la humedad de la piel, que consiste en aplicarle una composición

El problema planteado en esta solicitud es la necesidad de una composición para humectar la piel

Para resolver este problema técnico la solicitud en estudio proporciona una composición que contiene (a) humectante de estructura $(CH_3)(CH_3)(CH_3)N^+(CH_2)X$ en donde X es CH_2OH , $CHOHCH_2CO_2^-$ ó sus mezclas y (b) un vehículo compatible con la piel. Opcionalmente es un líquido, sólido, crema, loción ó gel, contiene ácido orgánico, tensioactivos, agente oclusivo

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El objeto de la invención definido anteriormente se clasificó de acuerdo con la IPC A 61 K 7/48

También se reivindica prioridad de la Solicitud de Patente de los Estados Unidos US 09 473 590 de diciembre 28 de 1999, con respecto a la cual la fecha de presentación de la actual solicitud cumple el plazo máximo permitido

3 Determinación del Estado de la Técnica

El artículo 16 de la decisión 486 de la comisión de la Comunidad Andina que establece que *"El estado de la técnica comprenderá todo lo que haya sido accesible al público por una descripción escrita u oral, utilización, comercialización o cualquier otro medio antes de la fecha de presentación de la solicitud de patente o, en su caso, de la prioridad reconocida"*

Solo para el efecto de la determinación de la novedad, también se considerará dentro del estado de la técnica, el contenido de una solicitud de patente en trámite ante la oficina nacional competente, cuya fecha de presentación o de prioridad fuese anterior a la fecha de presentación o de prioridad de la solicitud de patente que se estuviese examinando, siempre que dicho contenido esté incluido en la solicitud de fecha anterior cuando ella se publique o hubiese transcurrido el plazo previsto en el artículo 40"

Considerando que la fecha de presentación de la primera solicitud de patente de la cual se reivindica prioridad es diciembre 28 de 1999, se consultaron las bases de datos y los archivos con que cuenta la entidad con fecha de publicación anterior y se encontraron los siguientes documentos que anticipan el objeto de esta solicitud

No	Documento	Título	Fecha de Publicación
D1	US 4 885 157	Dermal Cosmetic Composition and Applications therefor	Dic 5, 1989
D2	WO 96 27363	Hair and Skin Treatment Agent	Sep 12, 1996
D3	US 5 571 518	Cosmetic Compositions Containing Tricholine Citrate	Nov 5, 1996

4 Evaluación de los requisitos de Patentabilidad

El artículo 14 de la Decisión 486 de la Comisión de la Comunidad Andina establece que *"Los Países Miembros otorgarán patentes para las invenciones, sean de producto o de procedimiento, en todos los campos de la tecnología, siempre que sean nuevas, tengan nivel inventivo y sean susceptibles de aplicación industrial"*

En cumplimiento del artículo 14 de la Decisión 486, se procedió a evaluar el cumplimiento de los requisitos de novedad, nivel inventivo y aplicación industrial, con el fin de establecer la patentabilidad de la invención reivindicada en la solicitud en estudio

Evaluación del Nivel Inventivo

El artículo 18 de la Decisión 486 de la Comisión de la Comunidad Andina establece que *Se considerará que una invención tiene nivel inventivo, si para una persona del oficio normalmente versada en la materia técnica correspondiente, esa invención no hubiese resultado obvia ni se hubiese derivado de manera evidente del estado de la técnica"*

Las reivindicaciones 1 – 18 se refieren a una composición que contiene (a) humectante de estructura (CH₃)X(CH₃)X(CH₃)N⁺(CH₂) X en donde X es CH₂OH, CHOHCH₂CO₂⁻ ó sus mezclas y (b) un vehículo compatible con la piel

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Opcionalmente es un líquido, sólido, crema, loción ó gel, contiene ácido orgánico, tensioactivos, agente oclusivo

Las reivindicaciones 19 - 21 se refieren al proceso para aumentar la humedad de la piel, que consiste en aplicarle una composición

D1 enseña (ver folios 98 y 99) una composición humectante para aplicación dérmica que contiene (a) humectante colina y (b) ácido orgánico alifático

D2 enseña (ver folios 101 - 103) una composición humectante que contiene (a) una sal de colina de un ácido inorgánico ó un ácido carboxílico y (b) un vehículo compatible con la piel

D3 enseña (ver folios 104 - 110) una composición humectante que contiene citrato de tricolina (TCC) y un vehículo compatible con la piel Enseña (columna 16) un método para tratar la apariencia arrugada, seca, envejecida que consiste en aplicar a la piel una composición Enseña (ver columna 13) que el mecanismo por el cual actúan colina y TCC es que estas compiten con colina H^+ y se hacen disponibles a las células para la síntesis de los fosfolípidos celulares

Se aclara que

La característica principal de la composición reivindicada es que contiene el humectante de estructura $(CH_3)(CH_3)(CH_3)N^+(CH_2)X$ en donde X es CH_2OH , $CHOHCH_2CO_2^-$, es decir colina De manera que la característica principal de la composición reivindicada, que es el humectante colina, se incluía normalmente en las composiciones de las anterioridades

Se observa que

- (a) debido a que el humectante colina, era conocido en las anterioridades, una persona de habilidades ordinarias en el arte incluiría fácilmente el compuesto a la preparación de la composición de esta solicitud,
- (b) las reivindicaciones de esta solicitud no mencionan una característica que conceda un efecto diferente o especial a las composiciones reivindicadas, que pueda considerarse como un aporte a la técnica, así que son obvias para una persona versada en la materia,
- (c) el problema planteado en esta solicitud que es la necesidad de una composición para humectar la piel se resuelve proporcionando una composición que contiene (a) humectante de estructura $(CH_3)(CH_3)(CH_3)N^+(CH_2)X$ en donde X es CH_2OH , $CHOHCH_2CO_2^-$ ó sus mezclas y (b) un vehículo compatible con la piel, es decir de la misma manera como se resolvía en las anterioridades,
- (d) el resultado obtenido es decir la composición que contiene (a) humectante de estructura $(CH_3)(CH_3)(CH_3)N^+(CH_2)X$ en donde X es CH_2OH , $CHOHCH_2CO_2^-$ ó sus mezclas y (b) un vehículo compatible con la piel, no es inesperado
- (e) no parece haberse superado un prejuicio técnico anterior, con la composición propuesta que contiene (a) humectante de estructura $(CH_3)(CH_3)(CH_3)N^+(CH_2)X$ en donde X es CH_2OH , $CHOHCH_2CO_2^-$ ó sus mezclas y (b) un vehículo compatible con la piel,

de manera que el objeto reivindicado no tiene nivel inventivo

Con respecto a las reivindicaciones 19 - 21 que se refieren al proceso para aumentar la humedad de la piel, que consiste en aplicarle una composición, se observa que con base en el método enseñado en D3 (columna 16) para tratar la apariencia arrugada, seca, envejecida que consiste en aplicar a la piel una composición, una persona de habilidades ordinarias en el arte hubiera llegado

de manera obvia proceso para aumentar la humedad de la piel que consiste en aplicarle una composición Así que el objeto de estas reivindicaciones no tiene nivel inventivo

8 Conclusión

En conclusión, los requisitos de patentabilidad de la presente solicitud están afectados así

Item	Documento	Reivindicaciones afectadas	Requisito que afecta
D1	US 4 885 157	1 - 21	Nivel inventivo
D2	WO 98 27383	1 - 21	Nivel inventivo
D3	US 5 571 518	1 - 21	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
 Jefe de la División de Nuevas Creaciones

El anterior requerimiento fue notificado por fijación en lista, de fecha
24 AGO 2003

CONCEPTO TÉCNICO No 1307	EXAMINADOR TÉCNICO Código 202007
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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

RADICACIÓN 0-97840

EDICTO No. 812

LA SECRETARÍA GENERAL AD-HOC
HACE SABER

Que esta Superintendencia profirió Resolución No 34884 de 20-DIC-2006 Que el contenido de la parte resolutive es como sigue El Superintendente de Industria y Comercio

RESUELVE

ARTICULO PRIMERO Negar el privilegio de patente de invención para la solicitud correspondiente a "COMPOSICION HUMECTANTE"

ARTICULO SEGUNDO Notificar personalmente el contenido de la presente resolución al doctor Ramiro Castro Duque, o a quien haga sus veces, en su calidad de apoderado de Colgate - Palmolive Company entregándole copia de la misma advirtiéndole que contra ella procede el recurso de reposición interpuesto ante el Superintendente de Industria y Comercio el momento de la notificación o dentro de los 5 días hábiles siguientes a ella

NOTIFÍQUESE Y CUMPLASE
Dada en Bogotá D.C. a los

20 DIC. 2006

EL SUPERINTENDENTE DE INDUSTRIA Y COMERCIO


JAIRO CASTRO DUQUE

Para notificar a los interesados se fija el presente EDICTO en lugar visible al público en la SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO por el término de (10) diez días hábiles contados a partir de las 8:00 a.m. de hoy

Secretaría General Ad-Hoc 10-ENE-2007
Secretaría General Ad Hoc
EDICTO No 812

Este edicto se desfilja hoy 23-ENE-2007 a las 4 30 p.m.