

ESCOBAR - URIBE ASOCIADOS

A B G A D O S

Carrera 11A No. 94-76 Of. 305 - P.O. Box 94948, Bogotá, Colombia, S.A.

Tel.: (371) 6162051 - 6162061 - 6161859 - 6161869

Fax: (371) 6161859

REGISTRARIA Y COMERCIO

Radicación: 91040581

Fecha: 02

Fecha (CD): 2001-04-29 15:27:35

Trámite: 1. 512 PATENTES E 1 RESOLUTO 329 COMPLETO

Expediente: 2000 DIVISION DE NUEVAS CREACIONES

2436/P

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO DIVISIÓN DE NUEVAS CREACIONES

E. S. D.

Re: Expediente No. 01-010.851
Solicitud de Patente en nombre de
THE PROCTER & GAMBLE COMPANY

Yo, JIMENA ESCOBAR URIBE, identificada como aparece al pie de mi firma, domiciliada en Bogotá, en la Carrera 11 A No. 94-76 Of. 305, obrando como apoderada de la sociedad THE PROCTER & GAMBLE COMPANY., solicitante de la patente de la referencia, anexo al presente memorial los siguientes documentos:

Copias certificadas de las solicitudes de Patentes Números 09/503168 y 09/503568 presentadas en Estados Unidos de América el día 14 de febrero del 2000, con las debidas traducciones de lo pertinente, incluyendo el capítulo reivindicatorio.

A este mismo respecto, debe tenerse en cuenta que en las primeras páginas de las copias en mención la Oficina de Patentes correspondiente certificó la fecha de presentación de esas solicitudes, cumpliéndose de esta forma todos y cada uno de los requisitos establecidos en el inciso segundo del artículo 10 de la Decisión 486 de la Comisión de la Comunidad Andina.

Señor Superintendente,


JIMENA ESCOBAR URIBE
C.C.39.779.452 de usaquén
T.P. 68.228
Cod. 5376

J5

**ESTADOS UNIDOS DE AMERICA
A TODOS AQUELLOS A QUIENES EL PRESENTE
LLEGUE:**

**DEPARTAMENTO DE COMERCIO DE LOS ESTADOS
UNIDOS
Oficina de Patentes y Marcas de los Estados Unidos**

diciembre 20, 2000

La presente es para certificar que el anexo es una copia fiel de los registros de la Oficina de Patentes y Marcas de los Estados Unidos, de los documentos de la solicitud de patente identificada más adelante, que cumplieron con los requerimientos para concederse una fecha de presentación de acuerdo con 35 USC 111.

Número de Solicitud: 09/503,568

Fecha de Presentación: febrero 14, 2000

Por la autoridad del
Comisionado de Patentes y Marca

(fdo) E. BORNETT
Oficial Certificador
Sello oficial de la Oficina de Patentes y Marcas de los
Estados Unidos de América

1. Una composición para proporcionar de forma tópica al menos un ingrediente farmacéuticamente activo que incluye:
 - a) Desde aproximadamente 1% hasta aproximadamente 50% en peso de al menos un fosfolípido.
 - b) Desde aproximadamente 0.01% hasta aproximadamente 10% de al menos un ingrediente farmacéuticamente activo.
 - c) Desde aproximadamente 0.01% hasta aproximadamente 0.5% en peso de al menos un agente quelante; y
 - d) Al menos un material de transporte apropiado seleccionado de los componentes utilizados en composiciones para aplicaciones tópicas.

En donde es dicho que al menos un agente acondicionador de la piel previene o reduce la resequedad, irritación y/o comezón de la piel de animales y/o humanos causada por la aplicación continua o repetitiva en la piel de dichos animales y/o humanos, de composiciones tópicas.

2. Una composición conforme a la Reivindicación 1 en donde dicho fosfolípido se selecciona del grupo formado por fosfolípidos insaturados, fosfolípidos parcialmente saturados y mezclas de ellos.
3. Una composición conforme a la Reivindicación 2 en donde dicho agente acondicionador de la piel se selecciona del grupo formado por vaselina, parafina líquida, cera de parafina, cera de abejas, .espermaceti, cera microcristalina, cetil alcohol, hexadecil alcohol, estearil alcohol, oleil alcohol, miristato de isopropilo, palmitato de isopropilo, aceite vegetal, esqualeno, esqualano, ácido palmítico, ácido esteárico, cetil palmitato, lanolina, tocoferol, acetato de tocoferol, glicerina, hexilenglicol,

propilenglicol, sorbitol, pantenol, poli alcoholes con 3-5 átomos de carbono, y mezclas de ellos.

4. Una composición conforme a la Reivindicación 3 en donde dicho fosfolípido incluye desde aproximadamente 1.5% hasta aproximadamente 40% en peso de dicho compuesto tópico.
5. Una composición conforme a la Reivindicación 4 en donde dicho fosfolípido se selecciona del grupo formado por lecitina, fosfatidilcolina, fosfatidiletanolamina, fosfatidilcerina, fosfatidilinositol, ácido fosfatídico, espingomielina, y mezclas de ellos.
6. Una composición conforme a la Reivindicación 5 en donde dicho acondicionador de la piel contiene desde aproximadamente 1% hasta aproximadamente 40% en peso de dicho compuesto tópico.
7. Una composición conforme a la Reivindicación 6 en donde dicho agente acondicionador de la piel se selecciona del grupo formado por glicerina, vaselina, pantenol, lanolina, y mezclas de ellos.
8. Una composición conforme a la Reivindicación 7 en donde dicho fosfolípido incluye desde aproximadamente 2% hasta aproximadamente 30% en peso de dicha composición tópica.
9. Una composición conforme a la Reivindicación 8 en donde dicho fosfolípido se selecciona del grupo formado por fosfatidilcolina, fosfatidiletanolamina, fosfatidilcerina, fosfatidilinositol, y mezclas de ellos.



10. Una composición conforme a la Reivindicación 9 en donde dicho agente acondicionador de la piel incluye desde aproximadamente 2% hasta aproximadamente 30% en peso de dicho compuesto tópico.
11. Una composición conforme a la Reivindicación 10 en donde dicho agente acondicionador de la piel se selecciona del grupo formado por glicerina, vaselina, y mezclas de ellos.
12. Una composición conforme a la Reivindicación 11 en donde dicho fosfolípido incluye desde aproximadamente 2.5% hasta aproximadamente 20% en peso de dicha composición tópica.
13. Una composición conforme a la Reivindicación 12 en donde dicho fosfolípido es fosfatidilcolina.
14. Una composición conforme a la Reivindicación 13 en donde dicho agente acondicionador de la piel incluye desde aproximadamente 3% hasta aproximadamente 20% en peso de dicho compuesto tópico
15. Una composición conforme a la Reivindicación 14 en donde dicho agente acondicionador de la piel es glicerina.

DA 364381



2428 42
39

THE UNITED STATES OF AMERICA

TO ALL TO WHOM THESE PRESENTS SHALL COME:

UNITED STATES DEPARTMENT OF COMMERCE

United States Patent and Trademark Office

December 20, 2000

**THIS IS TO CERTIFY THAT ANNEXED HERETO IS A TRUE COPY FROM
THE RECORDS OF THE UNITED STATES PATENT AND TRADEMARK
OFFICE OF THOSE PAPERS OF THE BELOW IDENTIFIED PATENT
APPLICATION THAT MET THE REQUIREMENTS TO BE GRANTED A
FILING DATE UNDER 35 USC 111.**

APPLICATION NUMBER: 09/503,568

FILING DATE: February 14, 2000



**By Authority of the
COMMISSIONER OF PATENTS AND TRADEMARKS**

E. Bornett

**E. BORNETT
Certifying Officer**

Please type a plus sign (+) inside this box -> [+]

02-15-00

PTOBB/05 (12/97)

Approved for use through 09/30/00, OMB 0651-0032

Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number

40

02/14/00
36830 U.S. PTO

02/14/00
36830 U.S. PTO

UTILITY PATENT APPLICATION TRANSMITTAL

Attorney Contact No.	7053	Total Pages	20
First name Inventor or Application Identifier			
THOMAS EDWARD HUETTER			
Express Mail Label No.			
EJ30100830US			

(Only for new nonprovisional applications under 37 CFR 1.53(b))

APPLICATION ELEMENTS

See MPEP Chapter 600 concerning utility patent application contents.

ADDRESS TO:

Assistant Commissioner for Patents
Box Patent Application
Washington, D.C. 20231

- ☒ Fee Transmittal Form
(Submit an original, and a duplicate for fee processing)
- ☒ Specification Total Pages [18]
(preferred arrangement set forth below)
 - Descriptive Title of the Invention
 - Cross References to Related Applications
 - Statement Regarding Fed sponsored R&D
 - Reference to Microfiche Appendix
 - Background of the Invention
 - Brief summary of the Invention
 - Brief Description of the Drawings (if filed)
 - Detailed Description
 - Claim(s)
 - Abstract of the Disclosure
- ☐ Drawing(s) (35 USC 113) Total Sheets ☐
- ☐ Oath or Declaration
 - ☐ Newly executed (original or copy)
 - ☐ Copy from a prior application (37 CFR 1.53(d))
(for continuation/divisional with Box 17 completed)
(Note Box 5 below)
- ☐ DELETION OF INVENTORS
Sign statement attached deleting inventor(s)
named in the prior application, see 37 CFR
1.53(d)(2) and 1.53(b).
- ☐ Incorporation By Reference (useable if Box 4b is checked)
The entire disclosure of the prior application, from which a
copy of the oath or declaration is supplied under Box 4b, is
considered as being part of the disclosure of the
accompanying application and is hereby incorporated by
reference therein.

- ☐ Microfiche Computer Program (Appendix)
- Nucleotide and/or Amino Acid Sequence Submission
(if applicable, all necessary)
 - ☐ Computer Readable copy
 - ☐ Paper Copy (identical to computer copy)
 - ☐ Statement verifying identity of above copies

ACCOMPANYING APPLICATION PARTS

- ☐ Assignment Papers (cover sheet & document(s))
- ☐ 37 CFR 3.73(b) Statement [+]
(when there is an assignee)
- ☐ English Translation Document (if applicable)
- ☐ Information Disclosure ☐ Copies of IDS
Statement (IDS)/PTO-1449 Citations
- ☐ Preliminary Amendment
- ☒ Return Receipt Postcard (MPEP 503)
(Should be specifically itemized)
- ☐ Small Entity ☐ Statement filed in prior application
Statement(s) Status still proper and desired
- ☐ Certified Copy of Priority Document(s)
(if foreign priority is claimed)
- ☐ Other.

17. If a CONTINUING APPLICATION, check appropriate box and supply the requisite information:

☐ Continuation ☐ Divisional ☐ Continuation-in-part (CIP) of prior application No.

18. CORRESPONDENCE ADDRESS

☐ Customer Number or Bar Code Label

or [+]
New correspondence address below

(Insert Customer No. or Attach bar code label
here)

NAME

Loy M. White

ADDRESS

The Procter & Gamble Company, Health Care Research Center (Box 1000), P.O. Box 8008

CITY

Mason

STATE

OH

ZIP CODE

45040-8008

COUNTRY

TELEPHONE

(613) 822-3683

FAX

(613) 822-3300

FEE TRANSMITTAL FORM

CLAIMS	(1) FOR	(2) NUMBER FILED	(3) NUMBER EXTRA	(4) RATE	(5) CALCULATION
TOTAL CLAIMS (37 CFR 1.18 (c))		15-20	0	x \$18.00 =	\$
INDEPENDENT CLAIMS (37 CFR 1.18 (c))		1-3	0	x \$78.00 =	\$
MULTIPLE DEPENDENT CLAIMS (if applicable) (37 CFR 1.18(d))				+ \$200.00 =	\$
				BASIC FEE (37 CFR 1.18(e))	\$800.00
				Total of above Calculations =	\$800.00
				Reduction by 80% for filing by small entity (Note 37 CFR 1.9, 1.27, 1.28)	
				TOTAL =	\$800.00

19. The Commissioner is hereby authorized to charge payment of the following fees associated with this communication or credit any overpayment to Deposit Account No. 16-2480. A duplicate copy of this sheet is enclosed.

- a. ☒ Any patent application filing fees required under 37 CFR 1.16.
- b. ☒ Any patent application processing fees under 37 CFR 1.17.

20. The Commissioner is hereby authorized to charge payment of the following fees during the pendency of this application or credit any overpayment to Deposit Account No. 16-2480. A duplicate copy of this sheet is enclosed.

- a. ☒ Any patent application processing fees under 37 CFR 1.17.
- b. ☐ The issue fee set in 37 CFR 1.18 at or before mailing of the Notice of Allowance, pursuant to 37 CFR 1.311(b).
- c. ☒ Any filing fees under 37 CFR 1.16 for presentation of extra claims.

21. The total number of duplicate copies enclosed is 5. The Commissioner is hereby authorized to make any additional copies of this sheet needed to accomplish the purposes provided for herein and to charge any fee for such copies to Deposit Account No. 16-2480.

22. SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT REQUIRED

NAME	Loy M. White
SIGNATURE	
DATE	February 14, 2000

"Express Mail" mailing label number E12571882000

Date of Deposit February 14, 2000

I hereby certify that this paper is being deposited with the United States Postal Service "Express Mail" Post Office to "Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to Assistant Commissioner for Patents, Washington, D.C. 20591.

Loy M. White

Assistant Commissioner for Patents



Assistant Commissioner for Patents

42 45

A COMPOSITION FOR TOPICAL DELIVERY OF A PHARMACEUTICALLY
ACTIVE AGENT

Thomas Edward Huetter

Paul Robert Tanner

The present invention relates to compositions comprising high levels of at least one phospholipid and at least one skin conditioning agent for the topical delivery of at least one pharmaceutically active agent. The at least one skin conditioning agent of the compositions of the present invention prevents or reduces the drying, irritation, and/or itching of the skin of animals and/or humans caused by the continuous or repetitive application of topical compositions to the skin of animals and/or humans, which contain high levels of phospholipids.

BACKGROUND

There has been much interest in recent years in devising ways to achieve efficient transdermal delivery of pharmaceutically active agents. It has been found that phospholipids offer the potential of improved transdermal drug delivery. It is known, for example, that liposomes made from phospholipids are able to facilitate the uptake of certain compounds across the skin barrier. Phospholipids are used in a wide variety of pharmaceutical compositions, as well as cosmetics and food products. Phospholipids are used in pharmaceutical compositions as dispersing, emulsifying, and stabilizing agents and are included in intramuscular, intravenous, parenteral, and topical compositions. Examples of topical compositions comprising phospholipids include U.S. Patent 5,064,655 (Uster, et al.), which discloses a topical liposome gel composition having a high viscosity for application and delivery of a drug active at a wound site or mucosal tissue site; U.S. Patent 5,945,409 (Crandall), which discloses topical compositions comprising phospholipids for moisturizing keratinous tissue of a human or animal; U.S. Patent 5,814,343 (Jones, et al.), which discloses a cosmetic composition comprising phospholipids for delivering a cosmetically-effective benefit agent to a target site on the skin and/or hair; U.S. Patent 5,654,337 (Roentsch, et al.), which discloses a topical composition comprising phospholipids useful in delivering pharmaceutically active

09503568-021400

agents through the skin; and U.S. Patent 5,869,090 (Rosenbaum), which discloses a topical composition comprising phospholipids as vehicles for the transdermal delivery of dehydroepiandrosterone (DHEA).

Typically phospholipids are used at low concentrations, e. g., at or below about 1% by weight of the topical composition, and are generally regarded as non-irritating and non-sensitizing. However, when phospholipids are used at concentrations greater than about 1% by weight of the topical composition, they may cause drying, irritation, or itching of the skin when the topical composition is continuously or repetitively applied to the skin of animals and/or humans.

10

SUMMARY OF THE INVENTION

15

The present invention relates to compositions for the topical delivery of at least one pharmaceutically active agent comprising from about 1% to about 50% by weight of at least one phospholipid, from about 0.1% to about 50% by weight of at least one skin conditioning agent, from about 0.01% to about 10% of at least one pharmaceutically active agent, and at least one suitable carrier material selected from components used in compositions for topical application. The at least one skin conditioning agent prevents or reduces the drying, irritation, and/or itching of the skin of animals and/or humans caused by the continuous or repetitive application of the topical composition to the skin of animals and/or humans. Compositions of the present invention may be in the form of emulsions, creams, lotions, ointments, gels, pastes, solutions, or any other suitable topical skin formulation.

20

DETAILED DESCRIPTION OF THE INVENTION

25

30

The present inventors have discovered that the drying, irritation, and/or itching of the skin, caused when topical compositions, having greater than about 1% by weight of a phospholipid compound, especially unsaturated or partially saturated phospholipid compounds, are continuously or repetitively applied to the skin of animals and/or humans, can be reduced or prevented by the addition of a safe and effective amount of at least one skin conditioning agent to these topical compositions. Such compositions are typically used for dermal or transdermal delivery of pharmaceutically active agent or agents. Therefore, the present invention relates to compositions for the topical delivery of at least one pharmaceutically active agent comprising from about 1% to about 50% by

weight of at least one phospholipid, from about 0.1% to about 50% by weight of at least one skin conditioning agent, from about 0.01% to about 10% of at least one pharmaceutically active agent, and at least one suitable carrier material selected from components used in compositions for topical application. The at least one skin conditioning agent prevents or reduces the drying, irritation, and/or itching of the skin of animals and/or humans caused by the continuous or repetitive application of the topical composition to the skin of animals and/or humans. Compositions of the present invention may be in the form of emulsions, creams, lotions, ointments, gels, pastes, solutions, or any other suitable topical skin formulation. Depending upon the intended use of the skin preparation, other components may be incorporated into the compositions. Such formulations may comprise topically acceptable carrier materials as are helpful.

As used herein, "topical application" means directly spreading, spraying or laying of a compound or composition onto epidermal tissue. Topical application can be achieved by rubbing, applicator pads, containers with applicator filaments, sprays, or any other convenient means.

As used herein, "safe and effective amount" means an amount of a substance, compound, or composition high enough to provide a significant positive modification of the condition to be treated, e. g., drying, irritation, and/or itching of the skin of an animal or human, but low enough to avoid serious side effects (at a reasonable benefit/risk ratio), within the scope of sound medical judgment. A "safe and effective amount" of the substance, compound, or composition may vary with the kind and amount(s) of other ingredients used in combination with the particular substance, compound, or composition, the condition being treated, the severity of the condition, the duration of the treatment, the nature of concurrent therapy, and like factors.

As used herein, "effective" means successful treatment resulting in slowing, halting, or reversing, e. g., healing, the adverse condition being addressed.

As used herein "comprising" means that the compositions of the present invention can contain other ingredients which are compatible with the compositions and which preferably do not substantially modify the compositions of the present invention. The term encompasses the terms "consisting of" and "consisting essentially of".

As used herein, "pastes" are liquids for topical application, preferably to the skin of an animal or human, whose viscosity is enhanced to the point that flow is largely inhibited by the presence of undissolved, as well as dissolved, solids.

As used herein, "gels" are semisolid systems of suspended inorganic particles or organic macromolecules interpenetrated by a liquid for topical application, preferably to the skin of an animal or human.

As used herein, "emulsions", "creams", and "lotions" are multiphase liquids for topical application, preferably to the skin of an animal or human, containing special components such as surfactants and/or thickeners that inhibit or delay the separation of the phases.

As used herein, "solutions" are single phase liquids substantially free of solids, but small amounts of haze or cloudiness may be tolerated, for topical application, preferably to the skin of an animal or human.

As used herein, "suitable carrier materials" may include components typically used in compositions for topical application, preferably to the skin of an animal or human, but are not limited to, solvents, emollients, emulsifiers, humectants, thickeners, antioxidants, chelating agents, dispensing agents, preservatives, buffers, fragrances, colorants, substances which are used for the microbial and chemical stabilization of the composition, and the like. Such carrier materials are well known to and easily selected by the skilled artisan.

The following provides a detailed description of the essential and non-essential components of the compositions of the present invention. All percentages and ratios used herein are by weight, and all measurements made at 25°C, unless otherwise specified.

25 Phospholipids

The compositions of the present invention comprise at least one phospholipid compound. Phospholipids useful in the compositions of the present invention may be selected by the skilled artisan according to the kind and amount(s) of other ingredients used in the compositions of the present invention, the condition being treated, the severity of the condition, the duration of the treatment, the nature of concurrent therapy, and like factors. However, the preferred phospholipids useful in the compositions of the

00503568-021400

present invention include all lipoidal constituents, natural and/or synthetic, saturated, partially saturated, or unsaturated, that contain phosphorus in their molecules. The more preferred phospholipids for use in the compositions of the present invention include, but are not limited to, lecithin, phosphatidylcholine, phosphatidylethanolamine, phosphatidylserine, phosphatidylinositol, phosphatidic acid, sphingomyelins, and mixtures thereof. While there are no particular limitations to the quality, purity, and/or saturation level of the phospholipids used, the phospholipids are preferably unsaturated or partially saturated, of high quality, pharmaceutical grade. A most preferred phospholipid for use in the compositions of the present invention is phosphatidylcholine.
 10 Phosphatidylcholine may be obtained as commercially available soya or egg phosphatidylcholine. More preferably the phosphatidylcholine for use in the compositions of the present invention is soya phosphatidylcholine. The amount of phospholipid used in the compositions of the present invention is typically from about 1% to about 50%, preferably from about 1.5% to about 40%, more preferably from about 2% to about 30%, most preferably from about 2.5% to about 20% by weight of the compositions of the present invention.
 15

Skin Conditioning Agents

The compositions of the present invention comprise at least one skin conditioning agent. Skin conditioning agents useful in the compositions of the present invention may be selected according to the kind and amount(s) of phospholipids and other ingredients used in the compositions of the present invention, the condition being treated, the severity of the condition, the duration of the treatment, the nature of concurrent therapy, and like factors. However, the preferred skin conditioning agents useful in the compositions of the present invention are those compounds that are safe and effective in preventing or reducing drying, irritation, and/or itching of the skin of animals and/or humans caused by the continuous or repetitive application of topical compositions to the skin of animals and/or humans, which contain high levels of phospholipids. Preferably the skin conditioning agents for use in the compositions of the present invention include, but are not limited to, petrolatum, liquid paraffin, paraffin wax, beeswax, spermaceti, microcrystalline wax, cetyl alcohol, hexadecyl alcohol, stearyl alcohol, oleyl alcohol, isopropyl myristate, isopropyl palmitate, vegetable oil, squalene, squalane, palmitic acid,
 20
 25
 30

47 50

stearic acid, cetyl palmitate, lanolin, tocopherol, tocopherol acetate, glycerin, hexylene glycol, propylene glycol, sorbitol, panthenol, polyalcohols having 3-5 carbon atoms, and mixtures thereof; more preferably the skin conditioning agents for use in the compositions of the present invention include glycerin, petrolatum, lanolin, panthenol, and mixtures thereof; most preferably the skin conditioning agent for use in the compositions of the present invention is glycerin.

While there are no particular limitations to the quality and/or purity of the skin conditioning agents used, the skin conditioning agents are preferably of high quality, pharmaceutical grade. The amount of skin conditioning agents used in the compositions of the present invention may vary according to the amount of phospholipids present in the compositions of the present invention, but is typically in the range of from about 0.1% to about 50%, preferably from about 1% to about 40%, more preferably from about 2% to about 30%, most preferably from about 3% to about 20% by weight of the compositions of the present invention.

Pharmaceutically Active Agents

The compositions of the present invention comprise at least one pharmaceutically active agent. Pharmaceutically active agents to be delivered topically and found useful in the compositions of the present invention include, but are not limited to, analgesic/anti-inflammatory agents such as aspirin, ibuprofen, ketoprofen, diclofenac, naproxen, indomethacin, piroxicam, flurbiprofen, meclofenamate, ketorolac, tenidap, tebufelone, and their derivatives, isomers, and salts; anti-infective agents such as penicillin, erythromycin, tetracycline, clotrimazole and their derivatives, isomers, and salts; anti-diabetics such as chlorpropamide, glymidine, insulin, and their derivatives, isomers, and salts; anti-arrhythmics such as moricizine, propranolol, amiodarone, and their derivatives, isomers, and salts; anti-coagulants such as heparin, warfarin, and their derivatives, isomers, and salts; poison antidotes such as amiphenazol, obidoxim chloride, D-penicillamin, tiopromin, and their derivatives, isomers, and salts; androgens or antiandrogens such as testosterone, yohimbe, and their derivatives, isomers, and salts; vitamins or nutrients such as folic acid and niacin; corticosteroids such as beclomethasone, fluticasone, dexamethasone, and their derivatives, isomers, and salts; anticholinergics such as atropine, ipratropium, and their derivatives, isomers, and salts;

09503568-021400

antihistamines such as brompheniramine, doxylamine, diphenhydramine, and their derivatives, isomers, and salts; ganglionic stimulants such as nicotine and its derivatives, isomers, and salts; vasoconstrictors such as pseudoephedrine, phenylpropanolamine, and their derivatives, isomers, and salts; methylxanthines such as caffeine, theophylline, and their derivatives, isomers, and salts; and mixtures thereof.

The particular pharmaceutically active agent(s) and amount of pharmaceutically active agent(s) used in the compositions of the present invention are selected to be safe and effective and may vary with the kind and amount(s) of other ingredients used in combination with the particular pharmaceutically active agent(s), the condition being treated, the severity of the condition, the duration of the treatment, the nature of concurrent therapy, and like factors. Typically, the amount of pharmaceutically active agent(s) used in the compositions of the present invention is from about 0.01% to about 10%, preferably from about 0.025% to about 8%, more preferably from about 0.05% to about 6%, most preferably from about 0.1% to about 4% by weight of the compositions of the present invention. The preferred pharmaceutically active agent(s) used in the compositions of the present invention comprises analgesic/anti-inflammatory agents selected from the group consisting of aspirin, ibuprofen, naproxen, indomethacin, piroxicam, flurbiprofen, meclofenamate, ketoprofen, ketorolac, diclofenac, tenidap, tebufelone, their derivatives, isomers, and salts, and mixtures thereof. The more preferred pharmaceutically active agent(s) used in the compositions of the present invention analgesic/anti-inflammatory agents selected from the group consisting of ibuprofen, naproxen, indomethacin, piroxicam, flurbiprofen, ketoprofen, ketorolac, diclofenac, their derivatives, isomers, and salts, and mixtures thereof. The most preferred pharmaceutically active agent(s) used in the compositions of the present invention analgesic/anti-inflammatory agents selected from the group consisting of ketoprofen, ibuprofen, diclofenac, naproxen, their derivatives, isomers, and salts, and mixtures thereof.

Water

Water employed in the compositions of the present invention should preferably be of low ion content and free of organic impurities. Typically, water comprises from about 2% to about 99%, preferably from about 20% to about 95%, more preferably from

about 40% to about 90%, most preferably from about 60% to about 85% by weight of the compositions of the present invention.

Carrier Materials

Carrier materials may or may not be used in the compositions of the present invention. If used, they may be selected from components typically used in compositions for topical application, preferably to the skin of an animal or human, i. e., emulsions, creams, lotions, ointments, gels, pastes, solutions, and the like. Typically, the carrier materials may be selected from polar and/or non-polar solvents such as glycerin, polyglycerin, glycerin esters, propylene glycol, polypropylene glycol, ethylene glycol, triethylene glycol, polyethylene glycol, diethylene glycol monoethyl ether, 1,3-butylene glycol, maltitol, benzyl alcohol, ethanol, ethyl acetate, heptane, canola oil, olive oil, mineral oil, water, and the like; emulsifiers/surfactants such as sodium, potassium, and triethanolamine salts of oleic and stearic acids, dioctyl sodium sulfosuccinate, sodium dodecyl sulfate, glycerol monooleate, glycerol monostearate, ethoxylated sorbitan esters such as Polysorbate 20, Polysorbate 65, and Polysorbate 80, polymers such as acrylates/C10-30 alkyl acrylate crosspolymers (Pemulen® TR-1, B.F. Goodrich), and the like; thickeners such as agar, carrageenan, food starch, modified starch, gelatin, gum arabic, guar gum, cellulose gel, carbomer (Carbopol®), hydroxyethylcellulose, hydroxypropyl methylcellulose, pectin, sodium carboxymethylcellulose, polyacrylic acid, polyvinyl alcohol, polyethylene glycol, and the like; antioxidants such as benzenesulfonic acid 4-[(3-(3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl)-1-oxopropyl) amino] monosodium salt (Tinogard™ AO-6, Ciba Specialty Chemical Co., High Point, NC), ascorbic acid, ascorbyl palmitate, butylated hydroxyanisole, butylated hydroxytoluene, hypophosphorous acid, monothioglycerol, propyl gallate, sodium formaldehyde sulfoxylate, sodium metabisulfite, sodium thiosulfate, sodium pyrosulfite, acetone sodium bisulfite, sulfur dioxide, t-butylhydroquinone, tocopherol, tocopherol polyethylene glycol succinate, octadecyl hydroxycinnamate, pentaerythrityl-tetrakis, di-t-amylhydroquinone, pyrocatechol, pyrogallol, nordihydroguaiaric acid, benzalkonium chloride, di-coco-dimethylammonium chloride, dilauryl thiodipropionate, methyl parahydroxybenzoate, propyl parahydroxybenzoate, and the like; chelating agents such as edetic acid (EDTA) and its salts including, edetate sodium, edetate disodium, and

09503568-021400

edotate trisodium, sodium hexametaphosphate, gentisic acid ethanolamide, oxyquinoline sulfate, citric acid, sodium citrate, thioglycolic acid, thiolactic acid, thioglycerol, and the like; dispersing agents, preservatives, buffers, fragrances, colorants, and the like.

Typically, these carrier materials may be present in the compositions of the present invention in amounts which provide their intended purpose. For example, solvents typically comprise from about 2% to about 99%, preferably from about 20% to about 95%, more preferably from about 40% to about 90% by weight of the compositions of the present invention; emulsifiers typically comprise from about 0.05% to about 20%, preferably from about 0.1% to about 15%, more preferably from about 0.3% to about 10% by weight of the compositions of the present invention; thickeners typically comprise from about 0.05% to about 10%, preferably from about 0.1% to about 7.5%, more preferably from about 0.2% to about 5% by weight of the compositions of the present invention; antioxidants typically comprise from about 0.01% to about 0.5%, preferably from about 0.02% to about 0.2%, more preferably from about 0.05% to about 0.15% by weight of the compositions of the present invention; chelating agents typically comprise from about 0.01% to about 0.5%, preferably from about 0.02% to about 0.2%, more preferably from about 0.05% to about 0.15% by weight of the compositions of the present invention; preservatives typically comprise from about 0.01% to about 5%, preferably from about 0.05% to about 3%, more preferably from about 0.1% to about 2% by weight of the compositions of the present invention; buffers typically comprise from about 0.01% to about 10%, preferably from about 0.1% to about 5%, more preferably from about 0.5% to about 2% by weight of the compositions of the present invention; fragrances typically comprise from about 0.01% to about 1%, preferably from about 0.05% to about 0.5%, more preferably from about 0.1% to about 0.3% by weight of the compositions of the present invention.

Examples

The following examples are provided as illustrations of the composition and methods of the present invention, but are not limitations of the scope of the present invention.

Example 1

050568-021400

	<u>Ingredient</u>	<u>Wt. %</u>
	Ketoprofen	2.00
	Phosphatidylcholine	8.00
	Glycerin	10.00
5	Sodium hydroxide (50%)	1.48
	Sodium phosphate, dibasic	0.10
	Sodium phosphate, monobasic	0.02
	Benzyl alcohol	0.53
	EDTA Disodium	0.10
10	Carbomer	0.90
	Fragrance	0.20
	Acrylates/C10-30 alkyl acrylate crosspolymer	0.10
	Water	76.57

15 Example 2

	<u>Ingredient</u>	<u>Wt. %</u>
	Naproxen	1.00
	Phosphatidylcholine	8.00
	Petrolatum	5.00
20	Sodium hydroxide (50%)	1.54
	Sodium phosphate, dibasic	0.10
	Sodium phosphate, monobasic	0.02
	Benzyl alcohol	0.53
	EDTA Disodium	0.05
25	Carbomer	0.50
	Acrylates/C10-30 alkyl acrylate crosspolymer	0.45
	Water	82.81

30 Example 3

	<u>Ingredient</u>	<u>Wt. %</u>
--	-------------------	--------------

	Diclofenac	1.00
	Phosphatidylcholine	6.00
	Lanolin	5.00
	Glycerin	5.00
5	Sodium hydroxide (50%)	1.54
	Sodium phosphate, dibasic	0.10
	Sodium phosphate, monobasic	0.02
	Benzyl alcohol	0.53
	EDTA Disodium	0.05
10	Carbomer	0.45
	Fragrance	0.20
	Acrylates/C10-30 alkyl acrylate crosspolymer	0.50
	Water	79.61

09503566-021400

15 In each of the above examples, the pharmaceutically active agent is added to most of the water and enough sodium hydroxide is added to the mixture to raise the pH to allow complete dissolution of the pharmaceutically active agent. The sodium phosphate salts, EDTA disodium, and benzyl alcohol are added to the solution containing the pharmaceutically active agent and the mixture is stirred until all the components are

20 dissolved. The phosphatidylcholine is added to the solution which is then stirred for at least 4 hours to insure liposomes are formed. The liposome solution is then filtered to achieve a selected size distribution of the liposomes. The petrolatum, lanolin, fragrance, and acrylates/C10-30 acrylate crosspolymer are added to the remaining amount of the water in a separate container which is agitated vigorously to form an emulsion. This

25 emulsion is then added to the liposomes and blended. Carbomer is added slowly to the mix along with the glycerin and the remainder of the sodium hydroxide. The liposome preparation is then agitated for at least 30 minutes until a smooth mixture of the proper viscosity is obtained.

30 While particular embodiments of the present invention have been described, it will be obvious to those skilled in the art that various changes and modifications to the present invention can be made without departing from the spirit and scope of the

invention. It is intended to cover, in the appended claims, all such modifications that are within the scope of this invention.

WHAT IS CLAIMED IS:

004120-89505 0 503568-021400

1. A composition for the topical delivery of at least one pharmaceutically active agent comprising:

- a) from about 1% to about 50% by weight of at least one phospholipid;
b) from about 0.1% to about 50% by weight of at least one skin conditioning agent;
c) from about 0.01% to about 10% of at least one pharmaceutically active agent; and
d) at least one suitable carrier material selected from components used in compositions for topical application;

wherein said at least one skin conditioning agent prevents or reduces the drying, irritation, and/or itching of the skin of animals and/or humans caused by the continuous or repetitive application of said topical composition to the skin of said animals and/or humans.

2. A composition according to Claim 1 wherein said phospholipid is selected from the group consisting of unsaturated phospholipids, partially saturated phospholipids, and mixtures thereof.

3. A composition according to Claim 2 wherein said skin conditioning agent is selected from the group consisting of petrolatum, liquid paraffin, paraffin wax, beeswax, spermaceti, microcrystalline wax, cetyl alcohol, hexadecyl alcohol, stearyl alcohol, oleyl alcohol, isopropyl myristate, isopropyl palmitate, vegetable oil, squalene, squalane, palmitic acid, stearic acid, cetyl palmitate, lanolin, tocopherol, tocopherol acetate, glycerin, hexylene glycol, propylene glycol, sorbitol, panthenol, polyalcohols having 3-5 carbon atoms, and mixtures thereof.

4. A composition according to Claim 3 wherein said phospholipid comprises from about 1.5% to about 40% by weight of said topical composition.

5. A composition according to Claim 4 wherein said phospholipid is selected from the group consisting of lecithin, phosphatidylcholine, phosphatidylethanolamine,

phosphatidylserine, phosphatidylinositol, phosphatidic acid, sphingomyelina, and mixtures thereof.

6. A composition according to Claim 5 wherein said skin conditioning agent comprises from about 1% to about 40% by weight of said topical composition.
7. A composition according to Claim 6 wherein said skin conditioning agent is selected from the group consisting of glycerin, petrolatum, panthenol, lanolin, and mixtures thereof.
8. A composition according to Claim 7 wherein said phospholipid comprises from about 2% to about 30% by weight of said topical composition.
9. A composition according to Claim 8 wherein said phospholipid is selected from the group consisting of phosphatidylcholine, phosphatidylethanolamine, phosphatidylserine, phosphatidylinositol, and mixtures thereof.
10. A composition according to Claim 9 wherein said skin conditioning agent comprises from about 2% to about 30% by weight of said topical composition.
11. A composition according to Claim 10 wherein said skin conditioning agent is selected from the group consisting of glycerin, petrolatum, and mixtures thereof.
12. A composition according to Claim 11 wherein said phospholipid comprises from about 2.5% to about 20% by weight of said topical composition.
13. A composition according to Claim 12 wherein said phospholipid is phosphatidylcholine.
14. A composition according to Claim 13 wherein said skin conditioning agent comprises from about 3% to about 20% by weight of said topical composition.

09503558-021400

15. A composition according to Claim 14 wherein said skin conditioning agent is glycerin.

004120-895E0560

57 ~~6~~

ABSTRACT

The present invention relates to compositions for the topical delivery of at least one pharmaceutically active agent comprising from about 1% to about 50% by weight of at least one phospholipid and from about 0.1% to about 50% by weight of at least one skin conditioning agent. The at least one skin conditioning agent prevents or reduces the drying, irritation, and/or itching of the skin of animals and/or humans caused by the continuous or repetitive application of topical compositions to the skin of animals and/or humans, which contain high levels of phospholipids.

09503568.021400

"Express Mail" mailing label number 2002080172

Date of Deposit February 14, 2003

I hereby certify that this specimen is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" mailing under 39 CFR 1.20 on the date indicated above and is addressed to Assistant Commissioner for Patent, Washington, D.C. 20534.

Law M. White 4130

Agent mailing specimen 2003

[Signature]

Signature of Agent mailing specimen

DEBPFCGLYCERINCOMPLMW.doc
7933app

DECLARATION COMBINED WITH POWER OF ATTORNEY

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled

A COMPOSITION FOR TOPICAL DELIVERY OF A PHARMACEUTICALLY ACTIVE AGENT
the specification of which

☐ is attached hereto.
☐ was filed on _____ as United States
Application No. _____ or
PCT International Application Number _____
and was amended on _____ (if applicable)

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in Title 37 Code of Federal Regulations §1.56.

I hereby claim foreign priority benefits under Title 35 United States Code §119(a)-(d) or §365(b) of any foreign application(s) for patent or inventor's certificate, or §365(a) of any PCT International application which designated at least one country other than the United States of America, listed below and have also identified below any foreign application for patent or inventor's certificate, or of any PCT international application having a filing date before that of the application on which priority is claimed:

Prior Foreign Application(s)			Priority Claimed	
(Number)	(Country)	(Day/Month/Year Filed)	☐ Yes	☐ No
_____	_____	_____	☐ Yes	☐ No
(Number)	(Country)	(Day/Month/Year Filed)	☐ Yes	☐ No

I hereby claim the benefit under Title 35, United States Code §119(e) of any United States provisional application(s) listed below.

Application Serial No.	Filing Date	Application Serial No.	Filing Date
------------------------	-------------	------------------------	-------------

I hereby claim the benefit under Title 35, United States Code §120 of any United States application(s), or §365(c) of any PCT International application designating the United States of America, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of Title 35, United States Code §112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations §1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application:

U.S. Parent Application Number	PCT Parent Number	Parent Filing Date (MM/DD/YYYY)	Parent Patent Number (If applicable)
--------------------------------	-------------------	---------------------------------	--------------------------------------

As named inventor, I hereby appoint the following registered practitioner(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith:

Attorney Name	Attorney Reg Number	Associate Power of Attorney Attached	
Loy M. White	43,262	☐ Yes	☒ No
Betty J. Zee	36,069	☐ Yes	☒ No
Angela Marie Stone	41,335	☐ Yes	☒ No
Brahm J. Corstange	34,804	☐ Yes	☒ No
Jacobus C. Rasser	37,043	☐ Yes	☒ No
T. David Reed	32,931	☐ Yes	☒ No
Timothy B. Guffey	41,048	☐ Yes	☒ No

59 92

SEND CORRESPONDENCE TO:

Loy M. White, Health Care Research Center (Box 1050)

The Procter & Gamble Company

(513) 622-3993

Name

Phone No.

P.O. Box 8006

Mason

Ohio

45040-8006

Street

City

State

Zip Code

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Full name of first joint inventor, if any Thomas Edward Huetter

Inventor's signature

Thomas Edward Huetter

2/14/00

Date

Residence 8239 Best Tree Drive, West Chester, OH 45069

Citizenship USA

Post Office Address The Procter & Gamble Company, Health Care Research Center

P. O. Box 8006, Mason, OH 45040-8006

Full name of sole or second joint inventor Paul Robert Tanner

Inventor's signature

Paul Robert Tanner

Feb 14, 2000

Date

Residence 1101 Seavine Court, Maineville, OH 45039

Citizenship USA

Post Office Address The Procter & Gamble Company, Sharon Woods Technical Center, Box 205

11510 Reed Hartman Highway, Cincinnati, OH 45241

Full name of third joint inventor, if any

Inventor's signature

Date

Residence

Citizenship

Post Office Address

Full name of fourth joint inventor, if any

Inventor's signature

Date

Residence

Citizenship

Post Office Address

Full name of fifth joint inventor, if any

Inventor's signature

Date

Residence

Citizenship

Post Office Address

**ESTADOS UNIDOS DE AMERICA
A TODOS AQUELLOS A QUIENES EL PRESENTE
LLEGUE:**

**DEPARTAMENTO DE COMERCIO DE LOS ESTADOS
UNIDOS
Oficina de Patentes y Marcas de los Estados Unidos**

diciembre 21, 2000

La presente es para certificar que el anexo es una copia fiel de los registros de la Oficina de Patentes y Marcas de los Estados Unidos, de los documentos de la solicitud de patente identificada más adelante, que cumplieron con los requerimientos para concederse una fecha de presentación de acuerdo con 35 USC 111.

Número de Solicitud: 09/503,168

Fecha de Presentación: febrero 14, 2000

**Por la autoridad del
Comisionado de Patentes y Marca**

**(fdo) L. EDELEN
Oficial Certificador
Sello oficial de la Oficina de Patentes y Marcas de los
Estados Unidos de América**

1. Un método para prevenir o reducir condiciones de la piel tales como resequedad, irritación y comezón, tanto en animales como en humanos, causada por la aplicación continua o repetitiva de una composición tópica a dicha piel animal o humana, que comprende la adición a dicha composición tópica, de una cantidad segura y efectiva de al menos un agente acondicionador de la piel en donde dicha composición tópica incluye al menos un fosfolípido en una cantidad mayor que aproximadamente 1% en peso de dicho compuesto tópico.
2. Un método conforme a la Reivindicación 1 en donde dicho agente acondicionador de la piel incluye desde aproximadamente 0.1% hasta aproximadamente 50% en peso de dicha composición tópica.
3. Un método conforme a la Reivindicación 2 en donde dicho agente acondicionador de la piel se selecciona del grupo formado por vaselina, parafina líquida, cera de parafina, cera de abejas, espermaceti, cera microcristalina, cetil alcohol, hexadecil alcohol, estearil alcohol, oleil alcohol, miristato de isopropilo, palmitato de isopropilo, aceite vegetal, esqualeno, esqualano, ácido palmítico, ácido esteárico, cetil palmitato, lanolina, tocoferol, acetato de tocoferol, glicerina, hexilenglicol, propilenglicol, sorbitol, pantenol, poli alcoholes con 3-5 átomos de carbono, y mezclas de ellos.
4. Un método conforme a la Reivindicación 1 en donde dicho acondicionador de la piel contiene desde aproximadamente 1% hasta aproximadamente 40% en peso de dicho compuesto tópico.
5. Un método conforme a la Reivindicación 4 en donde dicho agente acondicionador de la piel se selecciona del grupo formado por glicerina, vaselina, pantenol, lanolina, y mezclas de ellos.

6. Un método conforme a la Reivindicación 1 en donde dicho agente acondicionador de la piel incluye desde aproximadamente 2% hasta aproximadamente 30% en peso de dicho compuesto tópico.
7. Un método conforme a la Reivindicación 6 en donde dicho agente acondicionador de la piel se selecciona del grupo formado por glicerina, vaselina, y mezclas de ellos.
8. Un método conforme a la Reivindicación 1 en donde dicho agente acondicionador de la piel incluye desde aproximadamente 3% hasta aproximadamente 20% en peso de dicho compuesto tópico
9. Un método conforme a la Reivindicación 8 en donde dicho agente acondicionador de la piel es glicerina.
10. Un método conforme a la Reivindicación 1 en donde dicho fosfolípido incluye desde aproximadamente 1% hasta aproximadamente 50% en peso de dicho compuesto tópico.
11. Un método conforme a la Reivindicación 1 en donde dicho compuesto tópico incluye:
 - a) Desde aproximadamente 1% hasta aproximadamente 50% en peso de al menos un fosfolípido.
 - b) Desde aproximadamente 0.01% hasta aproximadamente 10% de al menos un ingrediente farmacéuticamente activo.
 - c) Desde aproximadamente 0.01% hasta aproximadamente 0.5% en peso de al menos un agente quelante; y
 - d) Al menos un material de transporte apropiado seleccionado de los componentes utilizados en composiciones para aplicaciones tópicas.
12. Un método conforme a la Reivindicación 11 en donde dicho fosfolípido se selecciona del grupo formado por fosfolípidos insaturados, fosfolípidos parcialmente saturados y mezclas de ellos.

13. Un método conforme a la Reivindicación 12 en donde dicho agente acondicionador de la piel se selecciona del grupo formado por vaselina, parafina líquida, cera de parafina, cera de abejas, espermaceti, cera microcristalina, cetil alcohol, hexadecil alcohol, estearil alcohol, oleil alcohol, miristato de isopropilo, palmitato de isopropilo, aceite vegetal, esqualeno, esqualano, ácido palmítico, ácido esteárico, cetil palmitato, lanolina, tocoferol, acetato de tocoferol, glicerina, hexilenglicol, propilenglicol, sorbitol, pantenol, poli alcoholes con 3-5 átomos de carbono, y mezclas de ellos.
14. Un método conforme a la Reivindicación 13 en donde dicho fosfolípido incluye desde aproximadamente 1.5% hasta aproximadamente 40% en peso de dicho compuesto tópico.
15. Un método conforme a la Reivindicación 14 en donde dicho fosfolípido se selecciona del grupo formado por lecitina, fosfatidilcolina, fosfatidiletanolamina, fosfatidilcerina, fosfatidilinositol, ácido fosfatídico, espingomielina, y mezclas de ellos.
16. Un método conforme a la Reivindicación 15 en donde dicho agente acondicionador de la piel incluye desde aproximadamente 1% hasta aproximadamente 40% en peso de dicho compuesto tópico.
17. Un método conforme a la Reivindicación 16 en donde dicho agente acondicionador de la piel se selecciona del grupo formado por glicerina, vaselina, pantenol, lanolina, y mezclas de ellos.
18. Un método conforme a la Reivindicación 17 en donde dicho fosfolípido incluye desde aproximadamente 2% hasta aproximadamente 30% en peso de dicho compuesto tópico.
19. Un método conforme a la Reivindicación 18 en donde dicho fosfolípido se selecciona del grupo formado por fosfatidilcolina,

64 ~~68~~
fosfatidiletanolamina, fosfatidilcerina, fosfatidilinositol,, y mezclas de ellos.

20. Un método conforme a la Reivindicación 19 en donde dicho agente acondicionador de la piel incluye desde aproximadamente 2% hasta aproximadamente 30% en peso de dicho compuesto tópico.
21. Un método conforme a la Reivindicación 20 en donde dicho agente acondicionador de la piel se selecciona del grupo formado por glicerina, vaselina, y mezclas de ellos.
22. Un método conforme a la Reivindicación 21 en donde dicho fosfolípido incluye desde aproximadamente 2.5% hasta aproximadamente 20% en peso de dicha composición tópica.
23. Un método conforme a la Reivindicación 22 en donde dicho fosfolípido es fosfatidilcolina.
24. Un método conforme a la Reivindicación 23 en donde dicho agente acondicionador de la piel incluye desde aproximadamente 3% hasta aproximadamente 20% en peso de dicho compuesto tópico
25. Un método conforme a la Reivindicación 24 en donde dicho agente acondicionador de la piel es glicerina

2925 65 60



THE UNITED STATES OF AMERICA

TO ALL TO WHOM THESE PRESENTS SHALL COME:

UNITED STATES DEPARTMENT OF COMMERCE

United States Patent and Trademark Office

December 21, 2000

**THIS IS TO CERTIFY THAT ANNEXED HERETO IS A TRUE COPY FROM
THE RECORDS OF THE UNITED STATES PATENT AND TRADEMARK
OFFICE OF THOSE PAPERS OF THE BELOW IDENTIFIED PATENT
APPLICATION THAT MET THE REQUIREMENTS TO BE GRANTED A
FILING DATE UNDER 35 USC 111.**

APPLICATION NUMBER: 09/503,168

FILING DATE: February 14, 2000



**By Authority of the
COMMISSIONER OF PATENTS AND TRADEMARKS**

L. Edelen

**L. EDELEN
Certifying Officer**

Please type a plus sign (+) inside this box → [+]

02-15-00

PTO/BAS (12/97)

Approved for use through 09/30/00. OMB 0651-0032

Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number

016 8 0 54835

UTILITY PATENT APPLICATION TRANSMITTAL

(Only for new nonprovisional applications under 37 CFR 1.53(b))

Attorney Docket No.

7052

Total Pages

16

First name Inventor or Application Identifier

PAUL ROBERT TANNER

Express Mail Label No.

EJ302100809US

09/503168

APPLICATION ELEMENTS

See MPEP Chapter 600 concerning utility patent application contents.

ADDRESS TO:

Assistant Commissioner for Patents

Box Patent Application

Washington, D.C. 20231

1. ☒ Fee Transmittal Form
(Submit an original, and a duplicate for fee processing)

2. ☒ Specification Total Pages [16]
(preferred arrangement set forth below)

- Descriptive Title of the Invention
- Cross References to Related Applications
- Statement Regarding Fed sponsored R&D
- Reference to Microfiche Appendix
- Background of the Invention
- Brief summary of the Invention
- Brief Description of the Drawings (if filed)
- Detailed Description
- Claim(s)
- Abstract of the Disclosure

3. ☒ Drawing(s) (35 USC 113) Total Sheets ☐

4. ☒ Oath or Declaration

- a. ☒ Newly executed (original or copy)
- b. ☐ Copy from a prior application (37 CFR 1.53(d))
(for continuation/divisional with Box 17 completed)
(Note Box 8 below)

I. ☐ DELETION OF INVENTORS

Signed statement attached deleting inventor(s)
named in the prior application, see 37 CFR
1.53(d)(2) and 1.33(b).

5. ☐ Incorporation By Reference (useable if Box 4b is checked)

- The entire disclosure of the prior application, from which a copy of the oath or declaration is supplied under Box 4b, is considered as being part of the disclosure of the accompanying application and is hereby incorporated by reference therein.

17. If a CONTINUING APPLICATION, check appropriate box and supply the requisite information:

☐ Continuation ☐ Divisional ☐ Continuation-in-part (CIP) of prior application No.

18. CORRESPONDENCE ADDRESS

☐ Customer Number or Bar Code Label

(Insert Customer No. or Attach bar code label here)

or ☒ New correspondence address below

NAME

Loy M. White

ADDRESS

The Procter & Gamble Company, Health Care Research Center (Box 1050), P.O. Box 8000

CITY

Mason

STATE

OH

ZIP CODE

45040-8000

COUNTRY

TELEPHONE

(513) 622-3363

FAX

(513) 622-3360

FEE TRANSMITTAL FORM

67 71

CLAIMS	(1) FOR	(2) NUMBER FILED	(3) NUMBER EXTRA	(4) RATE	(5) CALCULATIONS
	TOTAL CLAIMS (37 CFR 1.16 (d))	25-30	5	x \$18.00 =	\$ 90.00
	INDEPENDENT CLAIMS (37 CFR 1.16 (e))	1-3	0	x \$78.00 =	\$
	MULTIPLE DEPENDENT CLAIMS (if applicable) (37 CFR 1.16(d))			+ \$270.00 =	\$
				BASIC FEE (37 CFR 1.16(a))	\$690.00
				Total of above Calculations =	\$780.00
	Reduction by 50% for filing by small entity (Note 37 CFR 1.9, 1.27, 1.28).				
				TOTAL =	\$780.00

19. The Commissioner is hereby authorized to charge payment of the following fees associated with this communication or credit any overpayment to Deposit Account No. 18-2480. A duplicate copy of this sheet is enclosed.

- a. ☒ Any patent application filing fees required under 37 CFR 1.16.
- b. ☒ Any patent application processing fees under 37 CFR 1.17.

20. The Commissioner is hereby authorized to charge payment of the following fees during the pendency of this application or credit any overpayment to Deposit Account No. 18-2480. A duplicate copy of this sheet is enclosed.

- a. ☒ Any patent application processing fees under 37 CFR 1.17.
- b. ☐ The issue fee set in 37 CFR 1.18 at or before mailing of the Notice of Allowance, pursuant to 37 CFR 1.311(b).
- c. ☒ Any filing fees under 37 CFR 1.16 for presentation of extra claims.

21. The total number of duplicate copies enclosed is 5. The Commissioner is hereby authorized to make any additional copies of this sheet needed to accomplish the purposes provided for herein and to charge any fee for such copies to Deposit Account No. 18-2480.

22. SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT REQUIRED	
NAME	Loy M. White
SIGNATURE	
DATE	February 14, 2009

"Express Mail" mailing label number 95051902010

Date of Deposit February 14, 2009

I hereby certify that this paper is being deposited with the United States Postal Service "Express Mail" Post Office in Addisesset under 37 CFR 1.10 on the date indicated above and is addressed to Assistant Commissioner for Patents, Washington, D.C. 20591.

Loy M. White
Assistant Commissioner for Patents



68 ~~7~~

METHOD OF REDUCING OR PREVENTING SKIN IRRITATION

Paul Robert Tanner

Thomas Edward Huetter

5

The present invention relates to a method of preventing or reducing drying, irritation, and/or itching of the skin of animals and/or humans caused by the continuous or repetitive application of topical compositions to the skin of animals and/or humans, which contain high levels of phospholipids. The method of the present invention
10 comprises adding a safe and effective amount of a skin conditioning agent to compositions containing high levels of phospholipids.

BACKGROUND

There has been much interest in recent years in devising ways to achieve efficient transdermal delivery of pharmaceutically active agents. It has been found that
15 phospholipids offer the potential of improved transdermal drug delivery. It is known, for example, that liposomes made from phospholipids are able to facilitate the uptake of certain compounds across the skin barrier. Phospholipids are used in a wide variety of pharmaceutical compositions, as well as cosmetics and food products. Phospholipids are used in pharmaceutical compositions as dispersing, emulsifying, and stabilizing agents
20 and are included in intramuscular, intravenous, parenteral, and topical compositions. Examples of topical compositions comprising phospholipids include U.S. Patent 5,064,655 (Uster, et al.), which discloses a topical liposome gel composition having a high viscosity for application and delivery of a drug active at a wound site or mucosal tissue site; U.S. Patent 5,945,409 (Crandall), which discloses topical compositions
25 comprising phospholipids for moisturizing keratinous tissue of a human or animal; U.S. Patent 5,814,343 (Jones, et al.), which discloses a cosmetic composition comprising phospholipids for delivering a cosmetically-effective benefit agent to a target site on the skin and/or hair; U.S. Patent 5,654,337 (Roentseh, et al.), which discloses a topical composition comprising phospholipids useful in delivering pharmaceutically active
30 agents through the skin; and U.S. Patent 5,869,090 (Rosenbaum), which discloses a

004120-89TE05 0

topical composition comprising phospholipids as vehicles for the transdermal delivery of dehydroepiandrosterone (DHEA).

Typically phospholipids are used at low concentrations, e. g., at or below about 1% by weight of the topical composition, and are generally regarded as non-irritating and non-sensitizing. However, when phospholipids are used at concentrations greater than about 1% by weight of the topical composition, they may cause drying, irritation, or itching of the skin when the topical composition is continuously or repetitively applied to the skin of animals and/or humans.

SUMMARY OF THE INVENTION

The present invention relates to a method of preventing or reducing conditions of the skin, such as drying, irritation, and itching in animals or humans, caused by the continuous or repetitive application of a topical composition comprising greater than about 1% by weight of said topical composition of at least one phospholipid, to the skin of an animal or human. The method comprises adding a safe and effective amount of at least one skin conditioning agent to the topical composition.

DETAILED DESCRIPTION OF THE INVENTION

The present inventors have discovered that the drying, irritation, and/or itching of the skin, caused when topical compositions having greater than about 1% by weight of a phospholipid compound, especially unsaturated or partially saturated phospholipid compounds, are continuously or repetitively applied to the skin of animals and/or humans, can be reduced or prevented by the addition of a safe and effective amount of at least one skin conditioning agent to these topical compositions. Such compositions are typically used for dermal or transdermal delivery of pharmaceutically active agent or agents. Therefore, the present invention relates to a method of preventing or reducing drying, irritation, and/or itching of the skin of animals and/or humans caused by the continuous or repetitive topical application of emulsions, creams, lotions, ointments, gels, pastes, solutions, and the like to the skin of animals and/or humans, which contain greater than about 1% by weight of the composition, of at least one phospholipid.

The method of the present invention comprises adding a safe and effective amount of at least one skin conditioning agent preferably selected from the group consisting of glycerin, lanolin, petrolatum, panthenol, and mixtures thereof, to topical

09503168-021400

compositions containing greater than about 1% by weight of the composition, of at least one phospholipid. Preparations of the invention may be in the form of emulsions, creams, lotions, ointments, gels, pastes, solutions, or any other suitable topical skin formulation. Depending upon the intended use of the skin preparation, other components
 5 may be incorporated into the compositions. Such formulations may comprise topically acceptable carrier materials as are helpful.

As used herein, "topical application" means directly spreading, spraying or laying of a compound or composition onto epidermal tissue. Topical application can be achieved by rubbing, applicator pads, containers with applicator filaments, sprays, or any
 10 other convenient means.

As used herein, "safe and effective amount" means an amount of a substance, compound, or composition high enough to provide a significant positive modification of the condition to be treated, e. g., drying, irritation, and/or itching of the skin of an animal or human, but low enough to avoid serious side effects (at a reasonable benefit/risk ratio),
 15 within the scope of sound medical judgment. A "safe and effective amount" of the substance, compound, or composition may vary with the kind and amount(s) of other ingredients used in combination with the particular substance, compound, or composition, the condition being treated, the severity of the condition, the duration of the treatment, the nature of concurrent therapy, and like factors.

As used herein, "effective" means successful treatment resulting in slowing, halting, or reversing, e. g., healing, the adverse condition being addressed.
 20

As used herein "comprising" means that the compositions of the present invention can contain other ingredients which are compatible with the compositions and which preferably do not substantially modify the compositions of the present invention. The
 25 term encompasses the terms "consisting of" and "consisting essentially of".

As used herein, "pastes" are liquids for topical application, preferably to the skin of an animal or human, whose viscosity is enhanced to the point that flow is largely inhibited by the presence of undissolved, as well as dissolved, solids.

As used herein, "gels" are semisolid systems of suspended inorganic particles or
 30 organic macromolecules interpenetrated by a liquid for topical application, preferably to the skin of an animal or human.

71 78

As used herein, "emulsions", "creams", and "lotions" are multiphase liquids for topical application, preferably to the skin of an animal or human, containing special components such as surfactants and/or thickeners that inhibit or delay the separation of the phases.

5 As used herein, "solutions" are single phase liquids substantially free of solids, but small amounts of haze or cloudiness may be tolerated, for topical application, preferably to the skin of an animal or human.

As used herein, "suitable carrier materials" may include components typically used in compositions for topical application, preferably to the skin of an animal or human, but are not limited to, solvents, emollients, emulsifiers, humectants, thickeners, 10 antioxidants, chelating agents, dispersing agents, preservatives, buffers, fragrances, colorants, substances which are used for the microbial and chemical stabilization of the composition, and the like. Such carrier materials are well known to and easily selected by the skilled artisan.

15 The following provides a detailed description of the essential and non-essential components of the compositions of the present invention. All percentages and ratios used herein are by weight, and all measurements made at 25°C, unless otherwise specified.

Phospholipids

20 The compositions of the present invention comprise at least one phospholipid compound. Phospholipids useful in the compositions of the present invention may be selected by the skilled artisan according to the kind and amount(s) of other ingredients used in the compositions of the present invention, the condition being treated, the severity of the condition, the duration of the treatment, the nature of concurrent therapy, 25 and like factors. However, the preferred phospholipids useful in the compositions of the present invention include all lipoidal constituents, natural and/or synthetic, saturated, partially saturated, or unsaturated, that contain phosphorus in their molecules. The more preferred phospholipids for use in the compositions of the present invention include, but are not limited to, lecithin, phosphatidylcholine, phosphatidylethanolamine, 30 phosphatidylserine, phosphatidylinositol, phosphatidic acid, sphingomyelins, and mixtures thereof. While there are no particular limitations to the quality, purity, and/or

004720-89720560

saturation level of the phospholipids used, the phospholipids are preferably unsaturated or partially saturated, of high quality, pharmaceutical grade. A most preferred phospholipid for use in the compositions of the present invention is phosphatidylcholine. Phosphatidylcholine may be obtained as commercially available soya or egg
 5 phosphatidylcholine. More preferably the phosphatidylcholine for use in the compositions of the present invention is soya phosphatidylcholine. The amount of phospholipid used in the compositions of the present invention is typically from about 1% to about 50%, preferably from about 1.5% to about 40%, more preferably from about 2% to about 30%, most preferably from about 2.5% to about 20% by weight of the
 10 compositions of the present invention.

Skin Conditioning Agents

The compositions of the present invention comprise at least one skin conditioning agent. Skin conditioning agents useful in the compositions of the present invention may be selected according to the kind and amount(s) of phospholipids and other ingredients
 15 used in the compositions of the present invention, the condition being treated, the severity of the condition, the duration of the treatment, the nature of concurrent therapy, and like factors. However, the preferred skin conditioning agents useful in the compositions of the present invention are those compounds that are safe and effective in preventing or reducing drying, irritation, and/or itching of the skin of animals and/or
 20 humans caused by the continuous or repetitive application of topical compositions to the skin of animals and/or humans, which contain high levels of phospholipids. Preferably the skin conditioning agents for use in the compositions of the present invention include, but are not limited to, petrolatum, liquid paraffin, paraffin wax, beeswax, spermaceti, microcrystalline wax, cetyl alcohol, hexadecyl alcohol, stearyl alcohol, oleyl alcohol,
 25 isopropyl myristate, isopropyl palmitate, vegetable oil, squalene, squalane, palmitic acid, stearic acid, cetyl palmitate, lanolin, tocopherol, tocopherol acetate, glycerin, hexylene glycol, propylene glycol, sorbitol, panthenol, polyalcohols having 3-5 carbon atoms, and mixtures thereof; more preferably the skin conditioning agents for use in the compositions of the present invention include glycerin, petrolatum, lanolin, panthenol,
 30 and mixtures thereof; most preferably the skin conditioning agent for use in the compositions of the present invention is glycerin.

While there are no particular limitations to the quality and/or purity of the skin conditioning agents used, the skin conditioning agents are preferably of high quality, pharmaceutical grade. The amount of skin conditioning agents used in the compositions of the present invention may vary according to the amount of phospholipids present in the compositions of the present invention, but is typically in the range of from about 0.1% to about 50%, preferably from about 1% to about 40%, more preferably from about 2% to about 30%, most preferably from about 3% to about 20% by weight of the compositions of the present invention.

Pharmaceutically Active Agents

Phospholipids are useful in a wide variety of pharmaceutical compositions to deliver active ingredients across the skin barrier. Pharmaceutically active agents to be delivered topically and found useful in the compositions of the present invention include, but are not limited to, analgesic/anti-inflammatory agents such as aspirin, ibuprofen, ketoprofen, diclofenac, naproxen, indomethacin, piroxicam, flurbiprofen, meclofenamate, ketorolac, tenidap, tebufelone, and their derivatives, isomers, and salts; anti-infective agents such as penicillin, erythromycin, tetracycline, clotrimazole and their derivatives, isomers, and salts; anti-diabetics such as chlorpropamide, glymidine, insulin, and their derivatives, isomers, and salts; anti-arrhythmics such as moricizine, propranolol, amiodarone, and their derivatives, isomers, and salts; anti-coagulants such as heparin, warfarin, and their derivatives, isomers, and salts; poison antidotes such as amiphenazol, obidoxim chloride, D-penicillamin, tiopromin, and their derivatives, isomers, and salts; androgens or antiandrogens such as testosterone, yohimbe, and their derivatives, isomers, and salts; vitamins or nutrients such as folic acid and niacin; corticosteroids such as beclomethasone, fluticasone, dexamethasone, and their derivatives, isomers, and salts; anticholinergics such as atropine, ipratropium, and their derivatives, isomers, and salts; antihistamines such as brompheniramine, doxylamine, diphenhydramine, and their derivatives, isomers, and salts; ganglionic stimulants such as nicotine and its derivatives, isomers, and salts; vasoconstrictors such as pseudoephedrine, phenylpropanolamine, and their derivatives, isomers, and salts; methylxanthines such as caffeine, theophylline, and their derivatives, isomers, and salts; and mixtures thereof.

095031 8-021400

09503168-0214 0

The particular pharmaceutically active agent(s) and amount of pharmaceutically active agent(s) used in the compositions of the present invention are selected to be safe and effective and may vary with the kind and amount(s) of other ingredients used in combination with the particular pharmaceutically active agent(s), the condition being
 5 treated, the severity of the condition, the duration of the treatment, the nature of concurrent therapy, and like factors. Typically, the amount of pharmaceutically active agent(s) used in the compositions of the present invention is from about 0.01% to about 10%, preferably from about 0.025% to about 8%, more preferably from about 0.05% to about 6%, most preferably from about 0.1% to about 4% by weight of the compositions
 10 of the present invention. The preferred pharmaceutically active agent(s) used in the compositions of the present invention comprises analgesic/anti-inflammatory agents selected from the group consisting of aspirin, ibuprofen, naproxen, indomethacin, piroxicam, flurbiprofen, meclofenamate, ketoprofen, ketorolac, diclofenac, tenidap, tebupelone, their derivatives, isomers, and salts, and mixtures thereof. The more
 15 preferred pharmaceutically active agent(s) used in the compositions of the present invention analgesic/anti-inflammatory agents selected from the group consisting of ibuprofen, naproxen, indomethacin, piroxicam, flurbiprofen, ketoprofen, ketorolac, diclofenac, their derivatives, isomers, and salts, and mixtures thereof. The most preferred pharmaceutically active agent(s) used in the compositions of the present
 20 invention analgesic/anti-inflammatory agents selected from the group consisting of ketoprofen, ibuprofen, diclofenac, naproxen, their derivatives, isomers, and salts, and mixtures thereof.

Water

Water employed in the compositions of the present invention should preferably
 25 be of low ion content and free of organic impurities. Typically, water comprises from about 2% to about 99%, preferably from about 20% to about 95%, more preferably from about 40% to about 90%, most preferably from about 60% to about 85% by weight of the compositions of the present invention.

Carrier Materials

30 Carrier materials may or may not be used in the compositions of the present invention. If used, they may be selected from components typically used in

004T20-89T30560

compositions for topical application, preferably to the skin of an animal or human, i. e., emulsions, creams, lotions, ointments, gels, pastes, solutions, and the like. Typically, the carrier materials may be selected from polar and/or non-polar solvents such as glycerin, polyglycerin, glycerin esters, propylene glycol, polypropylene glycol, ethylene glycol, triethylene glycol, polyethylene glycol, diethylene glycol monoethyl ether, 1,3-butylene glycol, maltitol, benzyl alcohol, ethanol, ethyl acetate, heptane, canola oil, olive oil, mineral oil, water, and the like; emulsifiers/surfactants such as sodium, potassium, and triethanolamine salts of oleic and stearic acids, dioctyl sodium sulfosuccinate, sodium dodecyl sulfate, glycerol monooleate, glycerol monostearate, ethoxylated sorbitan esters such as Polysorbate 20, Polysorbate 65, and Polysorbate 80, polymers such as acrylates/C10-30 alkyl acrylate crosspolymers (Pennlen® TR-1, B.F. Goodrich), and the like; thickeners such as agar, carrageenan, food starch, modified starch, gelatin, gum arabic, guar gum, cellulose gel, carbomer (Carbopol®), hydroxyethylcellulose, hydroxypropyl methylcellulose, pectin, sodium carboxymethylcellulose, polyacrylic acid, polyvinyl alcohol, polyethylene glycol, and the like; antioxidants such as benzenesulfonic acid 4-[(3-(3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl)-1-oxopropyl) amino] monosodium salt (Tinogard™ AO-6, Ciba Specialty Chemical Co., High Point, NC), ascorbic acid, ascorbyl palmitate, butylated hydroxyanisole, butylated hydroxytoluene, hypophosphorous acid, monothioglycerol, propyl gallate, sodium formaldehyde sulfoxylate, sodium metabisulfite, sodium thiosulfate, sodium pyrosulfite, acetone sodium bisulfite, sulfur dioxide, t-butylhydroquinone, tocopherol, tocopherol polyethylene glycol succinate, octadecyl hydroxycinnamate, pentaerythrityl-tetrakis, di-t-amylhydroquinone, pyrocatechol, pyrogallol, nordihydroguaiaretic acid, benzalkonium chloride, di-coco-dimethylammonium chloride, dilauryl thiodipropionate, methyl parahydroxybenzoate, propyl parahydroxybenzoate, and the like; chelating agents such as edetic acid (EDTA) and its salts including edetate sodium, edetate disodium, and edetate trisodium, sodium hexametaphosphate, gentisic acid ethanolamide, oxyquinoline sulfate, citric acid, sodium citrate, thioglycolic acid, thiolactic acid, thioglycerol, and the like; dispensing agents, preservatives, buffers, fragrances, colorants, and the like.

Typically, these carrier materials may be present in the compositions of the present invention in amounts which provide their intended purpose. For example,

095031 8-021400

solvents typically comprise from about 2% to about 99%, preferably from about 20% to about 95%, more preferably from about 40% to about 90% by weight of the compositions of the present invention; emulsifiers typically comprise from about 0.05% to about 20%, preferably from about 0.1% to about 15%, more preferably from about 0.3% to about 10% by weight of the compositions of the present invention; thickeners typically comprise from about 0.05% to about 10%, preferably from about 0.1% to about 7.5%, more preferably from about 0.2% to about 5% by weight of the compositions of the present invention; antioxidants typically comprise from about 0.01% to about 0.5%, preferably from about 0.02% to about 0.2%, more preferably from about 0.05% to about 0.15% by weight of the compositions of the present invention; chelating agents typically comprise from about 0.01% to about 0.5%, preferably from about 0.02% to about 0.2%, more preferably from about 0.05% to about 0.15% by weight of the compositions of the present invention; preservatives typically comprise from about 0.01% to about 5%, preferably from about 0.05% to about 3%, more preferably from about 0.1% to about 2% by weight of the compositions of the present invention; buffers typically comprise from about 0.01% to about 10%, preferably from about 0.1% to about 5%, more preferably from about 0.5% to about 2% by weight of the compositions of the present invention; fragrances typically comprise from about 0.01% to about 1%, preferably from about 0.05% to about 0.5%, more preferably from about 0.1% to about 0.3% by weight of the compositions of the present invention.

Examples

The following examples are provided as illustrations of the composition and methods of the present invention, but are not limitations of the scope of the present invention.

Example 1

Ingredient	Wt. %
Ketoprofen	2.00
Phosphatidylcholine	8.00
Glycerin	10.00
Sodium hydroxide (50%)	1.48

17 8

	Sodium phosphate, dibasic	0.10
	Sodium phosphate, monobasic	0.02
	Benzyl alcohol	0.53
	EDTA Disodium	0.10
5	Carbomer	0.90
	Fragrance	0.20
	Acrylates/C10-30 alkyl acrylate crosspolymer	0.10
	Water	76.57

10 Example 2

	<u>Ingredient</u>	<u>Wt. %</u>
	Naproxen	1.00
	Phosphatidylcholine	8.00
	Petrolatum	5.00
15	Sodium hydroxide (50%)	1.54
	Sodium phosphate, dibasic	0.10
	Sodium phosphate, monobasic	0.02
	Benzyl alcohol	0.53
	EDTA Disodium	0.05
20	Carbomer	0.50
	Acrylates/C10-30 alkyl acrylate crosspolymer	0.45
	Water	82.81

	<u>Ingredient</u>	<u>Wt. %</u>
25	Diclofenac	1.00
	Phosphatidylcholine	6.00
	Lanolin	5.00
	Glycerin	5.00
30	Sodium hydroxide (50%)	1.54

004120-891E0560

0 503168 - 021400

Sodium phosphate, dibasic	0.10
Sodium phosphate, monobasic	0.02
Benzyl alcohol	0.53
EDTA Disodium	0.05
Carbomer	0.45
Fragrance	0.20
Acrylates/C10-30 alkyl acrylate crosspolymer	0.50
Water	79.61

10 In each of the above examples, the pharmaceutically active agent is added to most
of the water and enough sodium hydroxide is added to the mixture to raise the pH to
allow complete dissolution of the pharmaceutically active agent. The sodium phosphate
salts, EDTA disodium, and benzyl alcohol are added to the solution containing the
15 pharmaceutically active agent and the mixture is stirred until all the components are
dissolved. The phosphatidylcholine is added to the solution which is then stirred for at
least 4 hours to insure liposomes are formed. The liposome solution is then filtered to
achieve a selected size distribution of the liposomes. The petrolatum, lanolin, fragrance,
and acrylates/C10-30 acrylate crosspolymer are added to the remaining amount of the
water in a separate container which is agitated vigorously to form an emulsion. This
20 emulsion is then added to the liposomes and blended. Carbomer is added slowly to the
mix along with the glycerin and the remainder of the sodium hydroxide. The liposome
preparation is then agitated for at least 30 minutes until a smooth mixture of the proper
viscosity is obtained.

25 While particular embodiments of the present invention have been described, it
will be obvious to those skilled in the art that various changes and modifications to the
present invention can be made without departing from the spirit and scope of the
invention. It is intended to cover, in the appended claims, all such modifications that are
within the scope of this invention.

WHAT IS CLAIMED IS:

79 / 83

09503168-021400

1. A method of preventing or reducing conditions of the skin, such as drying, irritation, and itching in animals or humans, caused by the continuous or repetitive application of a topical composition to said skin of an animal or human, comprising adding a safe and effective amount of at least one skin conditioning agent to said
5 topical composition, wherein said topical composition comprises greater than about 1% by weight of said topical composition of at least one phospholipid.
2. A method according to Claim 1 wherein said skin conditioning agent comprises from about 0.1% to about 50% by weight of said topical composition.
3. A method according to Claim 2 wherein said skin conditioning agent is selected
5 from the group consisting of petrolatum, liquid paraffin, paraffin wax, beeswax, spermaceti, microcrystalline wax, cetyl alcohol, hexadecyl alcohol, stearyl alcohol, oleyl alcohol, isopropyl myristate, isopropyl palmitate, vegetable oil, squalene, squalane, palmitic acid, stearic acid, cetyl palmitate, lanolin, tocopherol, tocopherol acetate, glycerin, hexylene glycol, propylene glycol, sorbitol, panthenol, polyalcohols having 3-5 carbon atoms, and mixtures thereof.
4. A method according to Claim 1 wherein said skin conditioning agent comprises from about 1% to about 40% by weight of said topical composition.
5. A method according to Claim 4 wherein said skin conditioning agent is selected from the group consisting of glycerin, petrolatum, panthenol, lanolin, and mixtures thereof.
6. A method according to Claim 1 wherein said skin conditioning agent comprises from about 2% to about 30% by weight of said topical composition.
7. A method according to Claim 6 wherein said skin conditioning agent is selected from the group consisting of glycerin, petrolatum, and mixtures thereof.

80 

1

8. A method according to Claim 1 wherein said skin conditioning agent comprises from about 3% to about 20% by weight of said topical composition.
9. A method according to Claim 8 wherein said skin conditioning agent is glycerin.
10. A method according to Claim 1 wherein said phospholipid comprises from about 1% to about 50% by weight of said topical composition.
11. A method according to Claim 1 wherein said topical composition comprises:
 - a) from about 1% to about 50% by weight of at least one phospholipid;
 - b) from about 0.1% to about 50% by weight of at least one skin conditioning agent;
 - c) from about 0.01% to about 10% of at least one pharmaceutically active agent; and
 - d) at least one suitable carrier material selected from components used in compositions for topical application.
12. A method according to Claim 11 wherein said phospholipid is selected from the group consisting of unsaturated phospholipids, partially saturated phospholipids, and mixtures thereof.
13. A method according to Claim 12 wherein said skin conditioning agent is selected from the group consisting of petrolatum, liquid paraffin, paraffin wax, beeswax, spermaceti, microcrystalline wax, cetyl alcohol, hexadecyl alcohol, stearyl alcohol, oleyl alcohol, isopropyl myristate, isopropyl palmitate, vegetable oil, squalene, squalane, palmitic acid, stearic acid, cetyl palmitate, lanolin, tocopherol, tocopherol acetate, glycerin, hexylene glycol, propylene glycol, sorbitol, panthenol, polyalcohols having 3-5 carbon atoms, and mixtures thereof.
14. A method according to Claim 13 wherein said phospholipid comprises from about 1.5% to about 40% by weight of said topical composition.

9503168-021400

15. A method according to Claim 14 wherein said phospholipid is selected from the group consisting of lecithin, phosphatidylcholine, phosphatidylethanolamine, phosphatidylserine, phosphatidylinositol, phosphatidic acid, sphingomyelins, and mixtures thereof.
16. A method according to Claim 15 wherein said skin conditioning agent comprises from about 1% to about 40% by weight of said topical composition.
17. A method according to Claim 16 wherein said skin conditioning agent is selected from the group consisting of glycerin, petrolatum, panthenol, lanolin, and mixtures thereof.
18. A method according to Claim 17 wherein said phospholipid comprises from about 2% to about 30% by weight of said topical composition.
19. A method according to Claim 18 wherein said phospholipid is selected from the group consisting of phosphatidylcholine, phosphatidylethanolamine, phosphatidylserine, phosphatidylinositol, and mixtures thereof.
20. A method according to Claim 19 wherein said skin conditioning agent comprises from about 2% to about 30% by weight of said topical composition.
21. A method according to Claim 20 wherein said skin conditioning agent is selected from the group consisting of glycerin, petrolatum, and mixtures thereof.
22. A method according to Claim 21 wherein said phospholipid comprises from about 2.5% to about 20% by weight of said topical composition.
23. A method according to Claim 22 wherein said phospholipid is phosphatidylcholine.

82 8

24. A method according to Claim 23 wherein said skin conditioning agent comprises from about 3% to about 20% by weight of said topical composition.
25. A method according to Claim 24 wherein said skin conditioning agent is glycerin.

09503188.021400

83 84

ABSTRACT

The present invention relates to a method of preventing or reducing drying, irritation, and/or itching of the skin of animals and/or humans caused by the continuous or repetitive application of topical compositions to the skin of animals and/or humans, which contain high levels of phospholipids. The method of the present invention comprises adding a safe and effective amount of a skin conditioning agent to compositions containing high levels of phospholipids. The present invention further relates to compositions comprising high levels of a phospholipid and a skin conditioning agent.

"Express Mail" mailing label number 920210201721

Date of Deposit February 14, 2001

I hereby certify that this paperfile is being deposited with the United States Patent Service "Express Mail Post Office to Addressee" service under 37 CFR 1.9 on the date indicated above and is addressed to Assistant Commissioner for Patents, Washington, D.C. 20514.

Jan M. White ASAP
Agent making application Reg. No.

[Signature]
Signature of Agent making application

00503168-021400

DEHPGGLYCEBINMETHLMW.doc

DECLARATION COMBINED WITH POWER OF ATTORNEY

Page 1 of 2

Attorney Docket No. 7952

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled

METHOD OF REDUCING OR PREVENTING SKIN IRRITATION

the specification of which

☐ is attached hereto.
☐ was filed on _____ as United States
Application No. _____ or
PCT International Application Number _____
and was amended on _____ (if applicable)

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in Title 37 Code of Federal Regulations §1.56.

I hereby claim foreign priority benefits under Title 35 United States Code §119(a)-(d) or §365(b) of any foreign application(s) for patent or inventor's certificate, or §365(a) of any PCT International application which designated at least one country other than the United States of America, listed below and have also identified below any foreign application for patent or inventor's certificate, or of any PCT international application having a filing date before that of this application on which priority is claimed:

<u>Prior Foreign Application(s)</u>			<u>Priority Claimed</u>	
			☐	☐
			Yes	No
☐ (Number)	(Country)	(Day/Month/Year Filed)	☐	☐
☐ (Number)	(Country)	(Day/Month/Year Filed)	Yes	No

I hereby claim the benefit under Title 35, United States Code §119(e) of any United States provisional application(s) listed below.

<u>Application Serial No.</u>	<u>Filing Date</u>	<u>Application Serial No.</u>	<u>Filing Date</u>
-------------------------------	--------------------	-------------------------------	--------------------

I hereby claim the benefit under Title 35, United States Code §120 of any United States application(s), or §365(e) of any PCT International application designating the United States of America, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of Title 35, United States Code §112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations §1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application:

U.S. Parent Application Number	PCT Parent Number	Parent Filing Date (MM/DD/YYYY)	Parent Patent Number (If applicable)

As named inventor, I hereby appoint the following registered practitioner(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith:

<u>Atty Name</u>	<u>Atty Reg Number</u>	<u>Associate Power of Attorney Attached</u>	
Loy M. White	43,262	☐ Yes	☒ No
Betty J. Zee	36,069	☐ Yes	☒ No
Angela Marie Stone	41,335	☐ Yes	☒ No
Brahm J. Corstanje	34,804	☐ Yes	☒ No
Jacobus C. Rasser	37,043	☐ Yes	☒ No
T. David Reed	32,931	☐ Yes	☒ No
Timothy B. Guffey	41,048	☐ Yes	☒ No

85

SEND CORRESPONDENCE TO:

Loy M. White, Health Care Research Center (Box 1050)

The Procter & Gamble Company

(513) 622-3993

Name

Phone No.

P.O. Box 8006

Mason

Ohio

45040-8006

Street

City

State

Zip Code

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Full name of sole or first joint inventor Paul Robert Tanner

Inventor's signature Paul Robert Tanner

Feb 12, 2000

Date

Residence 1101 Seapine Court, Maineville, OH 45039

Citizenship USA

Post Office Address The Procter & Gamble Company, Sharon Woods Technical Center, Box 205

11510 Reed Hartman Highway, Cincinnati, OH 45241

Full name of second joint inventor, if any Thomas Edward Huetter

Inventor's signature Thomas Edward Huetter

2/14/00

Date

Residence 8239 Bent Tree Drive, West Chester, OH 45069

Citizenship USA

Post Office Address The Procter & Gamble Company, Health Care Research Center

P.O. Box 8006, Mason, OH 45040-8006

Full name of third joint inventor, if any _____

Inventor's signature _____

Date

Residence _____

Citizenship _____

Post Office Address _____

Full name of fourth joint inventor, if any _____

Inventor's signature _____

Date

Residence _____

Citizenship _____

Post Office Address _____

Full name of fifth joint inventor, if any _____

Inventor's signature _____

Date

Residence _____

Citizenship _____

Post Office Address _____