



No. 08-046044-00005-0000

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Act. 400 OPOSIOBSERVTER Folios: 58

FORMULARIO ÚNICO DE OPOSICIÓN

①

OPOSICIÓN A

- | | |
|---|---|
| ☒ Patente de Invención | ☐ Marca Colectiva |
| ☐ Patente de Modelo de Utilidad | ☐ Marca de Certificación |
| ☐ Diseño Industrial | ☐ Lema Comercial |
| ☐ Esquema de Trazado para Circuitos Integrados | |
| ☐ Marcas de Productos o Servicios | |

②

**SOLICITUD
PUBLICADA**

Numero del expediente: 08 046 044
Solicitante: BAYER CONSUMER CARE AG ✓
Apoderado: JAIME EDUARDO DELGADO VILLEGAS ✓
Titulo de la nueva creación o denominación del signo: _____
"USO DE COMPUESTOS DE CENTELLA ASIATICA"
Gaceta: 605

③ **OPOSICIÓN PRESENTADA POR:**

SOLICITANTE	Nombre: <u>GYNOPHARM S.A.</u>	IDENTIFICACION	
	Dirección: <u>Carrera 14 N° 94-44 Piso 7 Torre b</u> Nacionalidad o Domicilio: <u>COLOMBIA</u> Lugar de Constitución: <u>BARRANQUILLA</u>	C.C. ☐ C.E. ☐	NIT ☒ Otro ☐
	Teléfono: <u>2 36 84 95</u> Fax: _____ E-mail: _____	Cual: _____ Número: <u>802.006.279-4</u>	
REPRESENTANTE O APODERADO	Nombre: <u>CIELO ANGELA PEÑA RODRIGUEZ</u>	IDENTIFICACION	
	Dirección: <u>CARRERA 13 No. 119-95</u> Teléfono: <u>(571)213 12 13</u> Fax: <u>(571)612 19 79</u> E-mail: <u>negocios@optimum-co.com</u>	C.C. ☒ C.E. ☐	NIT ☐ Otro ☐
		Cual: _____ Número: <u>51.940.252</u> TP <u>82701</u>	

④ **FUNDAMENTOS DE LA OPOSICIÓN:**

Art. 14, 16, 18, 20 y 30 de la Decisión 486 de la CAN

Causal: No cumple con los requisitos de patentabilidad.

Signo opositor: _____

Justificación: _____

La presente solicitud no cumple con los requisitos de patentabilidad dado que lo revelado, ya se encontraba en el estado de la técnica o es posible derivarlo de la misma tal y como se demostrará en el capítulo "Fundamento de Hechos".

⑤ Comprobante de pago No. _____

Fecha _____

⑥ ANEXOS

- ☒ Comprobante de pago de la tasa.
- ☒ Poderes, si fuere el caso.
- ☒ Pruebas de los fundamentos de la oposición.
- ☐ Documentos que acrediten el legítimo interés, si fuere el caso.
- ☒ Documento que acredita la existencia y representación legal de las partes, cuando sean personas jurídicas.

⑦

NOMBRE: CIELO ANGELA PEÑA RODRIGUEZ ✓

FIRMA: 

C.C. 51.940.252

TP. 82701

Señora Jefe,

DIVISIÓN DE NUEVAS CREACIONES

Superintendencia de Industria y Comercio

E. S. D.

Referencia : Expediente N° 08 046.044
Asunto : Oposición a la solicitud de patente de Invención titulada
"USO DE COMPUESTOS DE CENTELLA ASIÁTICA"
Solicitante : BAYER CONSUMER CARE AG
Opositora : GYNOPHARM S.A.

Publicada en la Gaceta de la Propiedad Industrial
N° 605 del 30 de junio de 2009

Yo, **CIELO ANGELA PEÑA RODRIGUEZ**, abogada en ejercicio, identificada como aparece al pie de su firma, con tarjeta profesional No. **82701** del Consejo Superior de la Judicatura, en mi condición de apoderada de la sociedad **GYNOPHARM S.A.** conformada bajo las leyes de la Republica de Colombia y domiciliada en la ciudad de Barranquilla, Colombia, atentamente manifiesto que estando dentro del término de ley y por orden expresa de mi representada, presento oposición a la concesión del registro de la Patente de Invención titulada "USO DE COMPUESTOS DE CENTELLA ASIÁTICA", cuyo titular es BAYER CONSUMER CARE AG., y pido a Usted declarar fundada esta oposición y en consecuencia negar el registro de la patente solicitada.

1. INTERÉS PARA ACTUAR

Conforme a lo dispuesto en el artículo 42 de la Decisión 486 de 2000 de la CAN, estando dentro del término estipulado por la ley, manifiesto el legítimo interés de nuestra representada para oponerse al registro de la patente de la referencia, atendiendo a que la solicitud pretendida no cumple con los requisitos dispuestos en la ley como se analizará más adelante y de ser concedida afectaría directamente la comercialización de ~~algunos productos~~ de mi representada, que contienen, en particular compuestos de Centella asiática. Por lo tanto, solicito respetuosamente a ese Despacho se sirva tener en cuenta la presente oposición dentro del trámite administrativo que se surte en esta Superintendencia.

2. FUNDAMENTOS DE HECHOS

- 2.1. La solicitud objeto de la presente fue presentada el 9 de junio de 2006 reivindicando prioridad bajo la solicitud EP20050292384 del 2005-11-09; y fue publicada en Colombia, en la Gaceta de la Propiedad Industrial N° 605 del 30 de Junio de 2009, cuya publicación internacional corresponde a la WO2007/054211 del 18/05/2007.
- 2.2. La solicitud colombiana 08 046.044 objeto de la presente oposición, se refiere a un uso de al menos un compuesto de Centella asiática que se selecciona del grupo constituido por madecassósido, terminolósido, asiaticósido, ácido madecásico y ácido asiático para la fabricación de una composición para activar AQP-3, filagrina y/o transglutaminasa; uso para mejorar la diferenciación de queratinocitos y/o para potenciar la función epidérmica; uso para el tratamiento y/o prevención de anomalías de la maduración y/o queratinización epidérmicas; y uso para el

tratamiento de anomalías de la maduración y/o queratinización epidérmicas; para aumentar la cohesión del estrato córneo, la función de la barrera epidérmica y/o la impermeabilidad de la piel; y, para prevenir la deshidratación de la epidermis.

2.3. En primera instancia, se debe advertir que las reivindicaciones se refieren a un uso como método de tratamiento y no solo a la composición farmacológica o a un método de fabricación mediante la cual se obtenga un producto tangible y según la legislación, decisión 486 de la Comunidad Andina de Naciones, Artículo 14.- “Los Países Miembros otorgarán patentes para las invenciones, sean de producto o de procedimiento (...)”, los usos no están contemplados como patentables; y, Artículo 20.- “No serán patentables (...) d) los métodos terapéuticos o quirúrgicos para el tratamiento humano o animal, así como los métodos de diagnóstico aplicados a los seres humanos o a animales”. Solo serán patentables los productos o procedimientos. Por lo tanto a luz de la norma, dicha materia referente al uso y a un método de tratamiento no sería patentable.

2.4. Ahora bien, con base en el artículo 14 de la Decisión 486 de la CAN consagra lo siguiente: “Los países miembros otorgarán patentes para las invenciones, sean de producto o procedimiento, en todos los campos de la tecnología, siempre que sean nuevas, tengan nivel inventivo y sean susceptibles de aplicación industrial”. Así las cosas, las invenciones objeto de patente deben ser nuevas y tener nivel inventivo. Bien, pues antes de la fecha de prioridad de esta solicitud se encuentran los siguientes documentos que afecta la patentabilidad de la presente solicitud:

- D1: WO2005034891 publicada el 21 de abril de 2005.

2.5. Ahora bien, además que la presente se refiere a una materia que no es objeto de patente en Colombia, dichas caracterizaciones tampoco son novedosas, pues como

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lo indica el documento D1, particularmente en la descripción, revela una composición que puede prevenir los signos de envejecido, mejorar el aspecto estético de la piel que comprende al menos un ingrediente o extracto de Centella y al menos un vehículo farmacéuticamente o cosméticamente aceptable. Como tal dicha anterioridad revela tratamientos tales como la dermatitis y la atrofia de piel, microcirculación, humectación de la piel y elasticidad entre otros. Así las cosas, como lo evidencia dicho documento D1, la presente solicitud además no es novedosa pues lo revelado ya se encontraba en el estado de la técnica

2.6. En consecuencia y de acuerdo a lo descrito anteriormente, se deriva que la solicitud colombiana 08 046.044 no puede pretender un monopolio por patente toda vez que lo que pretende no cumple con dos de los tres requisitos necesarios para su protección.

2.7. Que por consiguiente, respecto a la solicitud pretendida se tiene que:

2.7.1. **CARECE DE NOVEDAD:** Según la decisión 486 de la Comunidad Andina de Naciones, Artículo 16.- *"Una invención se considerará nueva cuando no está comprendida en el estado de la técnica. El estado de la técnica comprenderá todo lo que haya sido accesible al público por una descripción escrita u oral, utilización, comercialización o cualquier otro medio antes de la fecha de presentación de la solicitud de patente o, en su caso, de la prioridad reconocida."* A la fecha de prioridad, 9 de septiembre de 2005 ya era conocido, pues como se demostró, era parte del arte anterior con base en el documento D1, una composición que puede prevenir los signos de envejecido, mejorar el aspecto estético de la piel que comprende al menos un ingrediente o extracto de Centella, sobre el cual busca protección en el capítulo reivindicatorio.

2.7.2. CARENCIA DE APLICACIÓN INDUSTRIAL La Decisión 486 de la CAN consagra en su artículo 14 lo siguiente: “*Los países miembros otorgarán patentes para las invenciones, sean de producto o procedimiento, en todos los campos de la tecnología, siempre que sean nuevas, tengan nivel inventivo y sean susceptibles de aplicación industrial*”. La presente solicitud carece de aplicación Industrial ya que como se demostró anteriormente, algunas cláusulas reclaman el método terapéutico y estos no son aplicables industrialmente porque primero no se obtiene un producto o proceso; y segundo no es reproducible o repetible a escala industrial. Por lo tanto, el objeto de la presente invención referido a los usos y métodos terapéuticos, no cumplen con el requisito de la aplicación industrial.

2.8. Dado lo anterior, es posible deducir que la solicitud y lo reivindicado no es objeto de patentabilidad pues es contrario a lo que dicta la Decisión 486 de la Comunidad Andina de Naciones, Artículo 14.- “*Los Países Miembros otorgarán patentes para las invenciones, sean de producto o de procedimiento, en todos los campos de la tecnología, siempre que sean nuevas, tengan nivel inventivo y sean susceptibles de aplicación industrial*”. La solicitud pretendida no cumple con dos de los tres requisitos de patentabilidad.

2.9. Por todo lo anterior, atentamente solicito a usted que se sirva declarar fundada la presente oposición y negar el registro Patente de invención denominada “**USO DE COMPUESTOS DE CENTELLA ASIATICA**”, cuyo titular es BAYER CONSUMER CARE AG, solicitud Colombiana que apareció publicada en la Gaceta de la Propiedad Industrial N° 605 del 30 de junio de 2009.

3. PRUEBAS

De conformidad con lo dispuesto por las normas vigentes, solicito a usted tener como prueba en este asunto los siguientes:

- D1: WO2005034891 publicada el 21 de abril de 2005.

4. FUNDAMENTO DE DERECHO

Fundamento esta observación en las normas legales siguientes:

- 4.1. Numeral 1 del artículo 586 del Código de Comercio.
- 4.2. Artículo 42 de la Decisión 486 de la Comisión del Acuerdo de Cartagena.
- 4.3. En las demás normas concordantes

5. ANEXOS

Para los efectos correspondientes anexo al presente escrito los siguientes documentos:

1. Poder para actuar en el presente.
 2. Documento que acredita al representante legal de **GYNOPHARM S.A.**
 3. Recibo de caja del respectivo pago de tasa.
 4. Copias de los documentos:
- D1: WO2005034891 publicada el 21 de abril de 2005.

6. NOTIFICACIONES

Para efectos de notificaciones que por disposición del artículo 50 del Decreto 01 de 1984 debe hacer su Despacho, informo que mi representante y la suscrita recibiremos notificaciones en la Secretaría de su Despacho o en mis oficinas situadas en la Carrera 13 N° 119-95, Of. 104 de esta ciudad de Bogotá.

Señor Superintendente,



CIELO ANGELA PEÑA RODRIGUEZ
C.C. 51'940.252 de Bogotá
T.P.A. 82701 del C.S. de la J.

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PODER ESPECIAL

Yo, **LUIS PALACIOS ARAGÓN**, mayor de edad y vecino de la ciudad de Barranquilla (Colombia), identificado como aparece al pie de mi firma, quien en el presente documento actúa en calidad de Representante Legal de la sociedad **GYNOPHARM S.A.** sociedad legalmente constituida y domiciliada en la ciudad de Barranquilla (Colombia), por el presente documento otorgo a la doctora **CIELO ANGELA PEÑA RODRIGUEZ**, abogada en ejercicio, identificada como aparece al pie de su firma, con tarjeta profesional No. 82701 del C.S. de la J., poder especial, amplio y suficiente, para formular oposiciones u observaciones a la solicitud de patente No. 08 046.044, titulada "USO DE COMPUESTOS DE CENTELLA ASIATICA", cuyo titular es **BAYER CONSUMER CARE AG**, publicada en la gaceta No. 605 del 30 de junio de 2009.

Nuestro apoderado queda facultado, de manera expresa, para realizar todo tipo de actos necesarios para llevar a cabo el trámite de la oposición, incluyendo, sin limitación, preparar y presentar solicitudes, hacer declaraciones, pagar tasas, contribuciones e impuestos, recabar los títulos o certificados. Asimismo quedan autorizados para impugnar administrativa y judicialmente todo lo que fuere resuelto en el expediente a que se hace expresa referencia en el presente poder, con todas las facultades generales y específicas que fuera requerido para ella.

De la misma manera, además de las facultades que le confiere la naturaleza del presente mandato, se encuentran facultados para recibir, desistir, transigir, sustituir, y reasumir el presente poder, incoar acciones, interponer recursos y demás facultades conferidas por la ley.

Dado y Firmado en Barranquilla (Colombia) a los 16 días del mes de setiembre de 2009.

GYNOPHARM S.A.

Cédula de Extranjería: No. 319788.

NIT: 802.006.279-4

Representante Legal

Acepto:

CIELO ANGELA PEÑA RODRIGUEZ

C.C. 51'940.252 de Bogotá

T.P.A. 82701 del C.S. de la J.

RECONOCIMIENTO DE DOCUMENTO PRIVADO

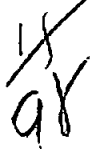
Ante mí, **WILMA ZAFRA TURBAY**, Notaria
Veinticinco **de** **Bogotá**, comparece

Señor **Alfonso Salazar**
1960
Identificado con cédula de ciudadanía

DE 319788
y declara que la firma puesta en el presente
instrumento privado es suya y que el contenido
del mismo es cierto. **17 SET. 2009**
Bogotá D.C.

FIRMA

WILMA ZAFRA TURBAY
NOTARIA VENTICINCO



8 3 7 3 5 0 3 5

0-9 A B C D E F G H I J K L M N O P Q R S T U V W X Y Z

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FECHA: 2009/08/13

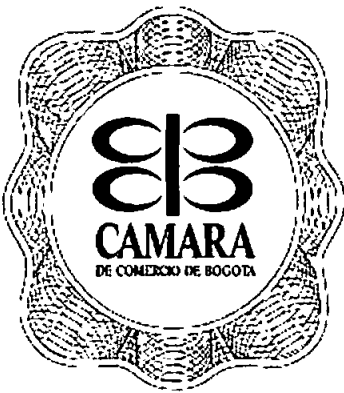
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uso y consumo humano y veterinario. b) La investigacion, desarrollo y fabricacion de toda clase de productos y sustancias quimicas, farmaceuticas y cosmeticas para uso y consumo humano, animal y vegetal. c) La compra y venta de materias primas, insumos y productos intermedios necesarios para los procesos de fabricacion de sustancias quimicas, farmaceuticas y cosmeticas, asi como la comercializacion interna y externa de los productos terminados. d) La compra, venta, importacion, exportacion y distribucion de toda clase de elementos instrumentales y equipos, medicos, quirurgicos, odontologicos y hospitalarios para la salud humana y animal. e) Actuar como representante o agente de personas naturales y juridicas nacionales y extranjeras en la realizacion de operaciones o transacciones relacionadas con la industria farmaceutica y en especial con cualesquiera de las actividades descritas en los literales a), b), c) y d) antes transcritos. f) Prestar los servicios de asesoria y consultoria en las areas administrativa, de mercadeo, analisis clinico, asistencia tecnica, investigacion, costos y produccion exportaciones, importaciones, ventas, relacionadas con iguales o similares actividades a las que constituyen el objeto de GYNOPHARM S.A., asi como los de publicidad y promocion de productos quimicos, cosmeticos y farmaceuticos para uso humano, animal o industrial. g) Adquirir, operar, administrar y explotar, a cualquier titulo, empresas o establecimientos dedicados a la investigacion, desarrollo, fabricacion o comercializacion de productos quimicos, farmaceuticos, hospitalarios o cosmeticos. En desarrollo de su objeto principal, la sociedad podra tomar interes social como accionista, socio o fundador de empresas que tengan igual o similar objeto; comprar, vender, importar y exportar maquinarias, insumos y repuestos requeridos para el desarrollo de sus actividades; tomar dinero en prestamo, financiar y garantizar las operaciones comerciales que celebre con terceros relativas a su objeto; celebrar y ejecutar todo tipo de actos y contratos necesarios para desarrollar sus operaciones; girar, aceptar, otorgar y protestar todo tipo de titulos valores e instrumentos negociables; comprar, vender y constituir gravámenes sobre bienes muebles e inmuebles; designar representantes o apoderados en el pais y en el exterior y, en

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pondan como representante legal por disposicion de la ley, de estos estatutos o de la junta directiva. El Gerente General tendra un suplente, designado por la junta directiva, quien lo reemplazara con identicas facultades en sus faltas temporales, absolutas o meramente accidentales, sin que sea necesario para ello acreditar la ausencia del principal.-----

C E R T I F I C A

Que según Acta No. 15 del 18 de Febrero de 2008 correspondiente a la Asamblea de Accionistas en Bogota, de la sociedad:

GYNOPHARM S.A.-----

cuya parte pertinente se inscribió en esta Cámara de Comercio, 1 25 de Febrero de 2008 bajo el No. 137,919 del libro respectivo, fueron hechos los siguientes nombramientos:

CLASE:

JUNTA DIRECTIVA

Principales

- | | |
|---|--------------------|
| 1. Llobet Poal Manuel | CC.*****14,670,196 |
| 2. Zanatta Reheman Leonardo Andres | CC.*****2,760,271 |
| 3. Munoz Marroquin Diego | CC.*****7,688,292 |
| 4. Montealegre Gonzalez Andres Leonardo | CC.*****79,950,262 |

Suplentes

- | | |
|-----------------------------------|--------------------|
| 1. Agudelo Pelaez Luis Hernando | CC.*****14,238,997 |
| 2. Aroca Almanza Arleth Ayelina | CC.*****36,718,415 |
| 3. Penaranda Urbina Adriana Paola | CC.*****53,120,683 |
| 4. tovar Vasquez Ruth | CC.*****52,175,756 |

C E R T I F I C A

Que según Acta No. 18 del 30 de Octubre de 2003 correspondiente a la Junta Directiva en Barranquilla, de la sociedad: GYNOPHARM S.A. cuya parte pertinente se inscribió en esta Cámara de Comercio, el 06 de Nov/bre de 2003 bajo el No. 107,783 del libro respectivo, fueron hechos los siguientes nombramientos:

Cargo/Nombre

Identificación

Gerente General.

Palacios Aragon Luis Alberto

CE.*****319,788

C E R T I F I C A

Que según Acta No. 49 del 03 de Marzo de 2008 correspondiente a la

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CERTIFICADO NACIONAL

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Junta Directiva en Barranquilla, de la sociedad: GYNOPHARM S.A. cuya parte pertinente se inscribió en esta Cámara de Comercio, el 11 de Marzo de 2008 bajo el No. 138,342 del libro respectivo, fueron hechos los siguientes nombramientos:

Cargo/Nombre	Identificación
Suplente del Gerente.	
Mollajoli Centurion Andres Fernando	CE.*****351,283

C E R T I F I C A

Que según Acta No. 19 del 30 de Abril de 2009 correspondiente a la Asamblea de Accionistas en Barranquilla, de la sociedad: GYNOPHARM S.A. cuya parte pertinente se inscribió en esta Cámara de Comercio, el 27 de Mayo de 2009 bajo el No. 149,314 del libro respectivo, fueron hechos los siguientes nombramientos:

Cargo/Nombre	Identificación
Revisor Fiscal.	
PENALOSA AUDITORES & ASOCIADOS S.A.	Ni.*****830,095,635

C E R T I F I C A

Que por Documento Privado del 11 de Mayo de 2009, otorgado en Bogota por Peñalosa Auditores & Asociados S.A. inscrito en esta Cámara de Comercio, el 27 de Mayo de 2009 bajo el Nro 149,315 del libro respectivo, fueron hechos los siguientes nombramientos:

Cargo/Nombre	Identificación
Designado: Revisor Fiscal Ppal	
Padilla Romero Ivan Dario	CC.*****80,025,798
Designado: Revisor Fiscal Suplente	
Gomez Preciado Clara Judith	CC.*****52,544,226

C E R T I F I C A

Que según Documento Privado de fecha 10 de Octubre del 2.000, inscrito en esta Camara de Comercio el 23 de Noviembre del 2.000 bajo el No. 1.872 del libro repectivo, consta que el señor RUBEN MINSKI GONTOVNIK C.C. No. 7.463.982, actuando como Presidente y representante legal de la sociedad GYNOPHARM S.A., otorga Poder Especial, Amplio y Suficiente a KAREN JENNIFER FIGUEROA GARCIA C.C. No. 32.-732.070, para que en nombre y representacion de la sociedad suscriba todas las: declaraciones cambiarias a que esta obligada GYNOPHARM

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CERTIFICADO NACIONAL

CAMARA DE COMERCIO DE BARRANQUILLA

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S.A., en el giro normal de sus negocios y operaciones sociales.-----

C E R T I F I C A

Que segun Documento Privado de fecha 10 de Octubre del 2.000, inscrito en esta Camara de Comercio el 12 de junio del 2.002, bajo el 2.164 del libro respectivo, consta que el señor JORGE CASTELLANOS MARTINEZ, identificado con C.C.No.19.460.089, actuando como representante legal de la sociedad GYNOPHARM S.A, otorga Poder Especial Amplio y Suficiente a KAREN FIGUEROA GARCIA, identificada con la cedula de ciudadanía No.32.732.070 de Barranquilla, mediante documento privado de octubre 10/2000, inscrito en la Camara de Comercio de Barranquilla bajo el No.1.872 del libro respectivo, para que en representacion de GYNOPHARM S.A, suscriba las declaraciones cambiarias a los que esta obligada GYNOPHARM S.A. en el giro ordinario de sus negocios y operaciones sociales.-----

C E R T I F I C A

Que por Escritura Pública No. 2,404 del 28 de Mayo de 2009, otorgada en la Notaria la. de Bogota cuya parte pertinente se inscribió en esta Cámara de Comercio, el 02 de Julio de 2009 bajo el No. 3,948 del libro respectivo,-----
consta que el señor LUIS ALBERTO PALACIOS ARAGON con CE No.319788, en su calidad de Representante Legal de GYNOPHARM S.A., manifesto que confiere poder general, amplio y suficiente a la Doctora -----
CAROLINA MARIA ROMERO CERON, identificada con cedula de ciudadanía numero 52.352.190, para que en nombre de la sociedad GYNOPHARM -----
S.A., promueva y defienda los intereses de la sociedad judicial y extrajudicialmente, en toda especie de gestiones y actuaciones ante las autooridades administrativas o jurisdiccionales en especial ----
para: a) Recibir notificaciones de cualesquiera tipo de actos -----
emanados de las autoridades administrativas o judiciales. b) -----
Presentar recursos por la via administrativa o judicial, renunciar a terminos, desistir, conciliar, transigir y modificar. c) Elevar peticiones y solicitar informacion a las autoridades -----
administrativas y jurisdiccionales. d) Presentar demandas ante las autoridades administrativas y judiciales.-----

C E R T I F I C A

*** CONTINUA ***



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CERTIFICADO NACIONAL

CAMARA DE COMERCIO DE BARRANQUILLA

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Que en esta Cámara de Comercio no aparecen inscripciones posteriores de documentos referentes a reforma, disolución, liquidación o nombramientos de representantes legales de la expresada sociedad.

C E R T I F I C A

Que su última Renovación fue el: 31 de Marzo de 2009.

La información sobre embargos de establecimiento se suministra en Certificados de Matrícula, la de contratos sujetos a registro, en Certificados Especiales.

C E R T I F I C A

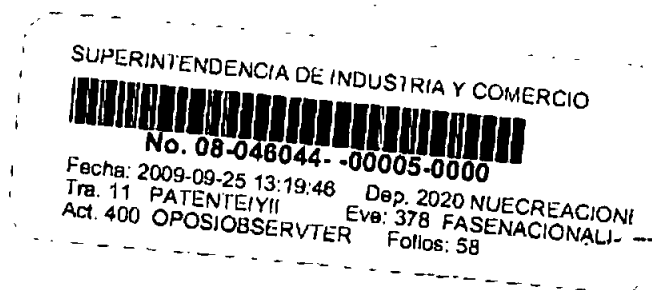
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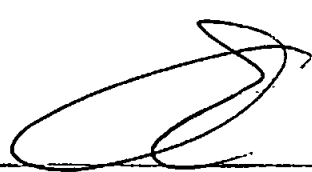
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(54) Title: COSMETIC COMPOSITION AND METHODS

(57) Abstract: A cosmetic composition is provided having ingredients that may prevent signs of aging, improve the aesthetic ap-
pearance of skin, and promote recovery from environmental stresses. The composition includes natural ingredients, including at least
one ingredient or extract from rosemary; at least one ingredient or extract from Centella, Echinacea, Alpinia or mixtures thereof; a
DNA repair enzyme; and at least one pharmaceutically or cosmetically acceptable vehicle.

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COSMETIC COMPOSITION AND METHODS

[0001] The present application claims priority to USSN 60/510,307 filed October 10, 2003, the entire contents of which are incorporated herein by reference.

BACKGROUND

[0002] The present invention relates to topical cosmetic compositions that incorporate materials to stimulate DNA repair mechanisms to repair skin cells. The disclosed compositions and methods may prevent, reduce, or reverse signs of premature aging, and/or improve the aesthetic appearance of skin. Use of the compositions may stimulate the skin's natural ability to recover from environmental stresses and prevent signs of premature aging. The compositions include natural active ingredients derived from natural plant materials, as well as enzymes for repairing DNA damage.

[0003] The skin is made up of two major layers. The stratum corneum, or epidermis, is the top or outer layer of the skin. The primary function of the stratum corneum is to provide a protective covering and retard evaporative water loss from the aqueous interior. This is commonly referred to as the barrier function. The stratum corneum protects against mechanical insults, the ingress of foreign chemicals and assaults by microorganisms. It also provides the first defense against ultraviolet light, screening out more than 80% of incident ultraviolet B irradiation.

[0004] The dermis lies under the epidermis and makes up 90 percent of the skin's thickness. The dermis contains a dense meshwork of collagen and elastin, providing strength and elasticity to the skin. Fibroblasts constitute the main cell type present in the dermis. Fibroblasts are responsible for synthesis and secretion of dermal matrix components, including collagen, elastin, and glycosaminoglycans (such as hyaluronic acid). Whereas collagen provides strength to the skin and elastin its elasticity, glycosaminoglycans serve to keep the skin moist and plump.

[0005] To stay healthy, the skin must cope with changing environmental conditions, while simultaneously repairing damage. Environmental factors play a chief role in

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aging, wrinkles, skin discolorations and degenerative skin conditions. Exposure to sunlight and UV radiation are major factors resulting in skin damage, accounting for 90% of the symptoms of premature aging. Importantly, exposure to oxygen, sunlight, and other environmental or lifestyle stresses induces the formation of free-radicals. Free radicals can cause wrinkles by activating metalloproteases, such as collagenases, that are responsible for breaking down the skin's connective tissues (collagen and elastin). The result is premature aging. Free-radical damage can also cause a reduction in the thickness of the dermal layer. This can cause the skin to slacken. The slackening of the skin is the first and most visible sign of aging and a cause of wrinkles and lines.

[0006] Sunlight also can cause the accumulation of abnormal elastin by triggering the overproduction of metalloproteinases. Normally, metalloproteinases remodel sun-injured skin by manufacturing and reforming collagen. Repeatedly subjecting the skin to this imperfect rebuilding process may lead to formation of wrinkles or solar scars. Exposure to the sun also can rob the skin of essential moisture and create a stressed barrier that does not function properly. As moisture loss and irritation increase, the skin becomes sensitive, scaly, and dry.

[0007] Although oxygen and sunlight constitute the principal sources of free-radical damage, other contributors include cigarette smoke, environmental toxins, herbicides, pesticides, weather, diet, stress, sleep deprivation, excessive alcohol consumption, and pollution.

[0008] UV radiation from the sun may also damage DNA and may bring about several detrimental effects including cell death, mutation and neoplastic transformation. Studies indicate that some of these deleterious effects are due to the formation of two major classes of bipyrimidine DNA photoproducts, cyclobutane pyrimidine dimers (CPDs) and (6-4) photoproducts (6-4 PPs). Organisms have evolved several different pathways for removing CPDs and 6-4 PPs from cellular DNA. These pathways include various excision repair pathways which can be highly specific or nonspecific for CPDs and 6-4 PPs.

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[0009] In view of the many detrimental effects impacting the skin, there is a demand for cosmetic compositions and cosmetic methods for improving the appearance and condition of skin. Consumers seek "anti-aging" cosmetic products that treat or delay the visible signs of actual aging and weathered skin, such as wrinkles, lines, sagging, hyperpigmentation and age spots. Consumers also seek other benefits from cosmetic products in addition to anti-aging benefits. For example, the concept of "sensitive skin" has raised the demand for cosmetic products that improve the appearance and condition of sensitive, dry and/or flaky skin, and that soothe red, and/or irritated skin. Consumers also desire cosmetic products that treat spots, pimples, blemishes, and the like, or that reduce the risk of skin cancer.

[0010] In spite of the various anti-aging cosmetic products on the market for the treatment of skin, there remains a need for effective topically applied cosmetic compositions that provide anti-aging or rejuvenating benefits to the skin, hair and/or nails using natural ingredients as active components. Unnatural, chemically-synthesized products may be perceived as being environmentally or personally unsafe. In contrast, natural products are perceived as pure, mild, and superior to chemically synthesized products. Natural based products extracted from plants or herbs are believed to contain antioxidant/free-radical scavenging agents that can neutralize the effects of free-radical damage. Additionally, they can contain agents that stimulate the synthesis and restoration of damaged connective tissue structures in the dermis and barrier function in the epidermis.

[0011] However, delivering a cosmetic benefit from "natural" sources, such as plants or herbs, is not trivial. Deriving a real benefit from such sources requires identification of specific plant/herbal extracts or ingredients, their minimum active concentrations, and their additive or synergistic activities in combination with other ingredients to impart anti-aging and/or skin improvement benefits.

[0012] The present compositions further address the frequent irritation problems associated with exfoliating agents such as retinoids (e.g., tretinoin, retinol and retinal), carboxylic acids including α -hydroxy acids (e.g., lactic acid, glycolic acid), β -hydroxy

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acids (e.g., salicylic acid), α -keto acids, acetic acid and trichloroacetic acid, 1-pyrrolidone-5-carboxylic acid, capryloyl salicylic acid, α -hydroxy decanoic acid, α -hydroxy octanoic acid, gluconolactone, methoxypropyl gluconamide, oxalic acid, malic acid, tartaric acid, mandelic acid, benzylic acid, gluconic acid, benzoyl peroxide and phenol, among others. Exfoliants and other ingredients may also increase the skin's sensitivity to environmental conditions such as sunlight, wind, cold temperature and dry air, or may exacerbate the irritation attributable to a pre-existing skin disease.

[0013] The present invention therefore provides cosmetic compositions for topical use that have anti-aging, anti-oxidant, anti-irritant, anti-inflammatory, and/or aesthetic improvement properties. The cosmetic compositions of the present invention may reduce irritation problems that may be encountered with conventional exfoliating agents.

BRIEF SUMMARY

[0014] In one embodiment, the present invention provides a topical composition including in a pharmaceutically or cosmetically acceptable vehicle, a *Rosmarinus officinalis* plant ingredient or extract; at least one plant ingredient or extract from *Centella*, *Echinacea*, *Alpinia*, or mixtures thereof; and a DNA repair enzyme

[0015] In a particular embodiment, the topical composition may include a *Rosmarinus officinalis* plant ingredient or extract; a *Centella asiatica* plant ingredient or extract; an *Echinacea angustifolia* plant ingredient or extract; an *Alpinia speciosa* plant ingredient or extract; and a liposome-encapsulated *Micrococcus luteus* N-glycosylase/AP lyase enzyme.

[0016] In another embodiment, the topical composition may include a *Rosmarinus officinalis* plant ingredient or extract; an *Alpinia speciosa* plant ingredient or extract; and a liposome-encapsulated *Micrococcus luteus* N-glycosylase/AP lyase enzyme.

[0017] The composition may include other cosmetically active plant or botanical ingredients present in, or in the form of, castor seed oil, Licorice root extract, seaweed extract, lemon extract, cucumber extract, sunflower seed extract, hydrolyzed oats, oat (*Avena sativa*) kernel extract, evening primrose extract (e.g., Lunawhite B), hydrolyzed

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soy protein, yeast extract (e.g., Toniskin), *Lentinus enodes* extract (e.g., Fermiskin), *Perilla ocymoides* leaf extract (e.g., Shiso extract), *Nymphaea alba* flower extract (e.g., Nympheline), silk proteins and/or combinations or derivatives thereof, and may further include a variety of vitamins, minerals, anti-oxidants and/or other cosmetically active agents. A suitable source for the plant or botanical ingredients is Barnet Products Corp., Englewood Cliffs, NJ.

[0018] The active ingredients may be obtained from seeds, needles, leaves, roots, bark, cones, stems, rhizomes, callus cells, protoplasts, organs and organ systems, or meristems. The active ingredients may be incorporated in the present compositions in a variety of forms. Such forms include a pure or semi-pure component, a solid or liquid (e.g. oil) extract or derivative, or a solid plant matter. The plant matter may also be incorporated in various subforms, including whole, minced, ground or crushed.

[0019] The present invention may also provide a method of improving the aesthetic appearance of skin, in which a composition of the present invention is topically applied to skin in a cosmetically effective amount. In a further aspect, the present invention provides a method to stimulate the skin's natural ability to recover from environmental stresses and/or prevent or reverse the signs of aging, in which a composition of the present invention is topically applied to skin areas typically exposed to UV rays or other environmental stresses.

[0020] The cosmetic composition of the present invention may be applied to the skin at a frequency of at least once a day. When the cosmetic composition is applied to the skin once a day, it is desirable to apply the composition in the evening so that further environmental insults to the skin are reduced. The cosmetic composition may be applied to skin for a period of time effective to provide anti-aging benefits and/or an improved aesthetic appearance. In one embodiment, the composition is applied at least once daily, for a period of fourteen days or longer.

[0021] The present invention also contemplates a kit suitable for a treatment regime to provide an amount of the cosmetic composition suitable for a desired period of time, such as fourteen days. According to this embodiment, a kit including a package that

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appearance of skin. Representative improvements may include, but are not limited to, favorable characteristics and/or properties related skin thickness, elasticity, resiliency, moisturization, smoothness, tone, texture, radiance, luster, brightness, clarity, contour, firmness, tautness, suppleness, softness, sensitivity, pore size, or combinations thereof. These terms may also be used to designate an improvement in an adverse skin condition. Representative adverse conditions affecting by, resulting in or resulting from such an adverse skin condition include, but are not limited to, psoriasis, eczema, seborrhea, dermatitis, sunburn, estrogen imbalance, hyperpigmentation, hypopigmentation, discoloration, yellowing, freckles, skin atrophy, skin breakout, skin fragility, dryness, tactile roughness, chapping, sagging, thinning, hyperplasia, fibrosis, enlarged pores, cellulite formation, bruising, acne formation, apoptosis, cellular differentiation, cellular de-differentiation, prevention of tumor induction or tumor progression, viral infections, fungal infections, bacterial infections, spider veins (telangiectasia), hirsutism, rosacea, pruritis, calluses, warts, corns, or combinations thereof.

[0034] The present invention provides a topical composition that includes, in a pharmaceutically or cosmetically acceptable vehicle, a *Rosmarinus officinalis* plant ingredient or plant extract; at least one plant ingredient or plant extract from *Centella*, *Echinacea*, *Alpinia*, or mixtures thereof; and a DNA repair enzyme.

[0035] Application of the topical composition of the present invention may improve the aesthetic appearance of the skin, and may rejuvenate or enhance the skin. The compositions of the present invention may also provide a variety of anti-aging and skin texture benefits. It is believed that the combination of ingredients used in the present invention provides significant anti-aging and skin texture benefits relative to the individual ingredients therein. Topical application of the ingredient combinations may produce benefits that are additive or synergistic relative to application of the individual ingredients therein.

[0036] The present invention may provide benefits to skin relating to anti-aging and improved aesthetic appearance. Accordingly, the present invention provides topical compositions and methods for their use in treating skin to prevent, arrest, reverse,

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ameliorate, diminish, reduce or improve signs of aging, including, or associated with, chronological aging, hormonal aging, and/or photoaging. The signs of aging may include, but are not limited to, skin fragility; loss of collagen and/or elastin; estrogen imbalance in skin; skin atrophy; appearance and/or depth of lines and/or wrinkles, including fine lines; skin discoloration, including dark eye circles; crow's feet; skin sagging; skin fatigue and/or stress, e.g., skin breakout due to environmental stress, such as pollution and/or temperature changes; skin dryness, fine lines due to skin dryness, skin roughness; skin flakiness; cellular aging; loss of skin tone, elasticity, clarity, luminosity, and/or luster; loss of skin firmness; poor skin texture; loss of skin elasticity and/or resiliency; thin skin, and inflammation.

[0037] The benefits and improvements to the aesthetic appearance of skin can be manifested in any of the following: reduction in pore size, fine lines, wrinkles, tactile roughness, and inflammation; improvement in skin tone, radiance, clarity and/or tautness; promotion of anti-oxidant activity; improvement in skin firmness, plumpness, suppleness, and/or softness; improvement in procollagen and/or collagen production; improvement in skin texture and/or promotion of retexturization; improvement in skin barrier repair and/or function; improvement in appearance of skin contours; restoration of skin luster, clarity, and/or brightness; replenishment of essential nutrients and/or constituents in the skin decreased by aging and/or menopause; improvement in communication among skin cells; increase in cell proliferation and/or multiplication; increase in skin cell metabolism decreased by aging and/or menopause; improvement in skin moisturization; promotion and/or acceleration of cell turnover; enhancement of skin thickness; increase in skin elasticity and/or resiliency; and enhancement of exfoliation, with or without the use of alpha or beta hydroxy acids, keto acids or other exfoliants.

[0038] Other benefits may include an increase in skin smoothness and/or softness, an increase in the perception of skin condition, an increase in skin moisture, a reduction in skin stress and fine lines, an increase in brightness, improved skin texture and skin firmness.

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[0039] In one embodiment of the present invention, the topical composition includes a plant ingredient or plant extract from *Rosmarinus officinalis* (Rosemary extract); at least one plant ingredient or plant extract from *Centella*, *Echinacea*, *Alpinia*, or mixtures thereof; a DNA repair enzyme; and a pharmaceutically or cosmetically acceptable vehicle.

[0040] Compositions of the present invention include an ingredient or extract from *Rosmarinus officinalis* (e.g., Rosemary extract). Ingredients from Rosemary are believed to have anti-aging, anti-cancer, anti-inflammatory, anti-microbial properties and/or low toxicity. Active ingredients in Rosemary are believed to include, but are not limited to, ursolic acid, carnosol, carnosic acid, rosmarinic acid and oleanolic acid. Active ingredients in *Rosmarinus officinalis* are believed to restore the skin's collagen bundle structures and elasticity, and/or to prevent or improve the appearance of lines, fine lines, wrinkles and/or age spots. Part of this appears to be attributed to ursolic acid and carnosic acid, which are believed to downregulate the enzymatic activity of metalloproteinase enzymes responsible for breakdown of collagen and elastin. Rosemary extract ingredients believed to function as anti-oxidants, include, but are not limited to carnosol, carnosic acid, rosmarinic acid and ursolic acid. Ursolic acid is believed to be a potent anti-inflammatory agent, to form oil-resistant barriers on the skin, and to improve the skin barrier function. Moreover, ursolic acid and oleanolic acid have also been shown to inhibit tumor promotion. Consequently, the use of these agents may provide the added benefit of protecting against the onset or promotion of skin cancer.

[0041] Other plant or botanical sources containing ursolic acid that may be used in the present invention include, but are not limited to, holy basil (tulsi; *Ocimum sanctum*), bilberry (*Vaccinium myrtillus*), devil's claw (*Harpagophytum procumbens*), elder flowers (*Sambucus nigra*), peppermint leaves (*Mentha piperita*), periwinkle (*Vinca minor*), lavender (*Lavendula angustifolia*), oregano (*Origanum vulgare*), thyme (*Thymus vulgaris*), hawthorn (*Crataegus laevigata*), cherry laurel leaves (*Prunus laurocerasus*), and ground ivy (*Glechoma hederacea*).

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[0042] The present invention may also include a plant ingredient or plant extract from *Centella*, *Echinacea*, *Alpinia*, or mixtures thereof. The ingredient or extract may be from any species members of these genus groups.

[0043] In a particular embodiment, the topical composition may include a *Rosmarinus officinalis* plant ingredient or extract; a *Centella asiatica* plant ingredient or extract; an *Echinacea angustifolia* plant ingredient or extract; an *Alpinia speciosa* plant ingredient or extract; and a liposome-encapsulated *Micrococcus luteus* N-glycosylase/AP lyase enzyme.

[0044] In another embodiment, the topical composition may include a *Rosmarinus officinalis* plant ingredient or extract; an *Alpinia speciosa* plant ingredient or extract; and a liposome-encapsulated *Micrococcus luteus* N-glycosylase/AP lyase enzyme.

[0045] *Centella* or *Centella asiatica* belongs to the *Hydrocotyl* genus and also is known as Gotu Kola or Indian Pennywort. *Centella asiatica* is believed to contain several active ingredients, including three triterpenes, asiatic acid, madecassic acid and asiaticoside. These ingredients are believed to be useful anti-wrinkle/anti-aging ingredients on account of several recognized properties. Specifically, *Centella* agents are believed to act upon connective tissue, where they are thought to increase collagen and glycosaminoglycan synthesis, increase connective tissue remodeling and elasticity, modulate fibroblast activity and/or metabolism, and act as an anti-inflammatory agent. Additionally, the *Centella* triterpenes have been found to dose-dependently inhibit free radical-induced collagen degradation. Of the three triterpenes, asiaticoside has been found to induce collagen synthesis and to elevate enzymatic and non-enzymatic anti-oxidant activities of vitamin E, vitamin C, superoxide dismutase, catalase, and glutathione peroxidase. *Centella* also is believed to have anti-inflammatory properties and has been used traditionally for treating eczema and for minor itching and insect bites.

[0046] *Echinacea* or coneflower is believed to exist in at least three varieties, *Echinacea purpurea*, *Echinacea angustifolia*, and *Echinacea pallida*. Total *Echinacea* extracts and echinoside, a caffeoyl derivative present therein, provide protective effects

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on skin connective tissue and are thought to enhance wound healing. Ingredients in *Echinacea* also are believed to possess anti-bacterial and anti-inflammatory activity and to reduce redness in skin or relieve conditions, such as eczema, insect bites and psoriasis.

[0047] *Alpinia* is a rhizomatous herb. Representative *Alpinia* members include, but are not limited to, *Alpinia galanga*, *Alpinia katsumadai*, *Alpinia officinalis*, *Alpinia oxyphylla*, *Alpinia purpurata*, *Alpinia speciosa*, and *Alpinia zerumbet*. *Alpinia* species are believed to promote collagen synthesis and cell growth and to inhibit activity of the collagenase and/or elastase enzymes, which breaks down collagen and elastin in process regulated by the NF- κ B pathway. Accordingly, a diarylheptanoid from *Alpinia officinarum* was recently shown to inhibit proinflammatory mediators via inhibition of mitogen activated protein kinase, p44/42 and transcription factor NF- κ B (J. Pharmacol. Exp. Ther., 305:925-931; see also Intl. J. Cosmetic Science, 21(2):71, April 1999). Advantageously, *Alpinia* extracts have been also found to inhibit tumor progression. Consequently, use of *Alpinia* ingredients or extracts may protect against skin cancer. Other compositions of the present invention may include *Alpinia speciosa*.

[0048] The plant ingredients or plant extracts for use in the present invention may be present in a collective amount ranging from about 0.0001% to 5% by weight of the total composition, desirably from about 0.001 wt % to about wt 0.5%, more desirably from about 0.01 wt % to about 0.1 wt %.

[0049] Rosemary extract, or ingredients thereof, may be present in an amount from about 0.001% to about 10% by weight of the composition. Desirably, the Rosemary ingredient or extract is present in an amount from about 0.05 wt % to about 5 wt %, more desirably from 0.01 wt % to about 1 wt %, and still more desirably from about 0.01 wt % to about 0.05 wt %, of the total weight of the composition.

[0050] The present invention may include a plant ingredient or plant extract from *Centella* or *Alpinia* (or mixtures thereof), where the at least one plant ingredient or plant extract is present in the composition, individually or collectively, in an amount ranging from about 0.001% to about 10% by weight of the total composition, desirably from

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about 0.005 wt % to about 2 wt %, more desirably from about 0.02 wt % to about 0.08 wt %. Alternatively, or in addition, the present invention may also include an ingredient or extract from either of the *Echinacea species*, where the ingredient or extract is present in the composition, individually or collectively, in an amount ranging from about 0.0001% to about 1% by weight of the total composition, desirably from about 0.001 wt % to about 0.1 wt %, more desirably from about 0.0005 wt % to about 0.02 wt %.

[0051] The plant ingredients of the present invention may be provided separately from a plant extract or they may be included with a plant extract present in a mixture. For example, *Rosmarinus officinalis* leaf extract with lecithin and water is available as MEROSPHERES from Applied Genetics, Inc. Dermatics, Freeport, NY. *Alpinia speciosa* leaf extract in water and butylene glycol is available as ALPINIA LEAF EXTRACT BG from Maruzen Pharmaceuticals Co., Ltd., Hiroshima, Japan. A combination of *Centella asiatica* extract, *Echinacea angustifolia* extract, and *Rosmarinus officinalis* leaf extract in dipropylene glycol and SD-alcohol is available as ACTIFIRM ULTRA DiPG from Active Organics, Lewisville, TX. Desired embodiments of the present invention may include at least one plant ingredient or plant extract from at least two, or more desirably three members of the group including, *Centella asiatica*, *Echinacea angustifolia*, and *Alpinia speciosa*.

[0052] DNA repair enzymes for use in the present invention may include enzymes involved in either the base excision repair (BER), the nucleotide excision repair (NER) pathway, or alternate excision repair pathways as described in e.g., U.S. Pat. No. 6,368,594. These pathways are mediated by separate sets of proteins capable of carrying out DNA incision, lesion removal, gap-filling, and ligation reactions.

[0053] The NER pathway constitutes a widely distributed, lesion non-specific repair pathway orchestrating DNA damage removal via a dual incision reaction upstream and downstream from the damage site resulting in release of an oligonucleotide containing the damage. Following removal of the damaged DNA, the resulting gap is filled and the DNA ends are ligated together.

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[0054] The BER pathway is the primary defense against all major forms of DNA base damage. This pathway is responsible for detecting and removing a variety of specific, individual base lesions within a large pool of undamaged DNA. BER pathways typically involve the activity of N-glycosylase/AP lyase enzymes specific for CPDs. The N-glycosylase/AP lyase enzymes first cleave the N-glycosidic bond of a CPD 5' pyrimidine and then cleave the phosphodiester backbone at an abasic site via a β -lyase mechanism.

[0055] Suitable DNA repair enzymes for use in the present invention have N-glycosylase/AP lyase activities capable of recognizing, excising and repairing damaged DNA, such as CPDs and (6-4) photoproducts. The activity of these enzymes can be light-dependent (e.g., photolyases) or light-independent. Exemplary DNA repair enzymes in this group include, but are not limited to, bacteriophage T4 pyrimidine dimer-specific endonuclease (denV endonuclease), *Micrococcus luteus* N-glycosylase/AP lyase, *Saccharomyces cerevisiae* N-glycosylase/apurinic-apyrimidinic lyase, *Schizosaccharomyces pombe* UV damage endonuclease (UVDE), *Chlorella virus* isolate PBCV-1 pyrimidine dimer-specific glycosylase, *Anacystis nidulans* photolyase, and modified, non-native (e.g., recombinant) enzyme products thereof.

[0056] DNA repair enzymes may also include other members from the BER, NER or alternate pathways. These enzymes may include O⁶-methylguanine-DNA methyltransferases, uracil- and hypoxanthine-DNA glycosylases, DNA exonucleases, damaged-bases glycosylases (e.g., 3-methyladenine-DNA glycosylase), endonucleases alone or in complexes (e.g., *E. coli* uvrA/uvrB/uvrC endonuclease complex), and other enzymes and enzyme complexes whose activities at present are only partially understood, such as, the products of the ERCC genes of humans and the RAD genes of yeast. Exemplary DNA repair enzymes include, but are not limited to, uracil DNA glycosylases, 3-methyladenine DNA glycosylase, Endonuclease III/thymine glycol DNA glycosylases, Endonuclease VIII, fapy/8-oxoguanine DNA glycosylases, A-G-mismatch DNA glycosylases, G-T mismatch DNA glycosylases, formyluracil DNA glycosylases, hydroxymethyl uracil DNA glycosylases, XPC-hHR23B, XPA, RPA, XPB, TFIIH, XPG, XPF-ERCC1, Rad4-Rad23, Rad14, Rfa, Rad25/Ss12, Rad3, Rad2, Rad1-Rad10,

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various DNA polymerases, DNA ligases and the like. Exemplary sources for these enzymes may include bacterial or mammalian cell sources, including, but not limited to *E. coli*, *S. cerevisiae*, *S. pombe*, human, human, monkey, mouse, rat, hamster and the like.

[0057] As used herein, the term "DNA repair enzyme" is intended to include the foregoing enzymes and other enzymes now known or subsequently discovered or developed, including glycosylases, apurinic/apyrimidinic endonucleases or other enzymes having activities capable of repairing damaged DNA.

[0058] DNA repair enzymes of the present invention may be derived or extracted from suitable sources such as *E. coli*, *Micrococcus*, and the like. The DNA repair enzymes may be encapsulated in liposomes as described in US 5,296,231, the entire contents of which is incorporated herein by reference. For example, a DNA repair enzyme derived from a *Micrococcus luteus* cell lysate is provided in a liposomal formulation containing lecithin and water and is available as ULTRASOMES™ from Applied Genetics, Inc. Dermatics, Freeport, NY or ULTRASOMES-V™ from Barnet Products Corporation, Englewood Cliffs, NJ. Liposomes encapsulating an *Anacystis nidulans* lysate containing the *Anacystis nidulans* photolyase are available as PHOTOSOMES™ from Applied Genetics, Inc. Dermatics, (Freeport, NY). The liposomes may include conventional phospholipids, oleic acid and/or cholesterol hemisuccinate from vegetable-derived sources, e.g., soybean or they may be produced from other suitable sources conventionally known to those skilled in the art.

[0059] Exemplary embodiments may incorporate ULTRASOMES™, ULTRASOMES-V™, or PHOTOSOMES™ in an amount ranging from about 0.01 % to 20 % by weight of the total composition, desirably from about 0.1 wt % to about wt 10 %, more desirably from about 0.5 wt % to about 3 wt %.

[0060] Liposomes may be used as delivery agents to facilitate transfer of cosmetically active agents into the dermis of skin, such as the DNA repair enzymes or the plant or botanical ingredients of the present invention. Other delivery agents may be used for dermal delivery in place of the liposomes, including, but not limited to skin

delivery vehicles known to those skilled in the art, including emulsions, microemulsions, nanoemulsions, nanoparticles, microspheres, ethosomes, transfersomes, and niosomes.

[0061] Additional cosmetic ingredients may also be included in the cosmetic composition of the present invention, including, but not limited to, ingredients present in: licorice, licorice extracts, licorice derivatives (e.g., glycyrrhizates); lemon extract; cucumber extract; sunflower seed extract; castor seed oil; oat proteins, oat extracts, hydrolyzed oats; silk protein (e.g., sericin); hyaluronic acid and its derivatives (e.g., sodium hyaluronate); vitamins; minerals; anti-oxidants; phospholipids, sphingolipids, cholesterol; and/or other ingredients or combinations thereof having anti-aging, anti-oxidant, anti-inflammatory, anti-irritant, anti-cancer or other skin-protective properties, aesthetic appearance enhancing properties, and/or increased skin delivery properties.

[0062] Cosmetically useful vitamins, minerals and/or anti-oxidants for topical application in accordance with the present invention include plant ingredients and extracts having anti-oxidant properties (e.g., Rosemary extract, Centella asiaticoside, etc.); vitamin A and its precursors or derivatives (e.g., beta-carotene, retinyl palmitate); vitamin B3 and its precursors or derivatives (e.g., niacinamide); vitamin B5 and its precursors or derivatives (e.g. panthenol); vitamin C and its precursors or derivatives (e.g., tetrahexyldecyl ascorbate, ascorbyl palmitate); vitamin E and its precursors or derivatives (e.g., d-alpha-tocopherol, tocopheryl acetate); vitamin K and its precursors or derivatives; selenium and its derivatives (e.g., L-selenomethionine); and alpha lipoic acid (ALA).

[0063] ALA is a potent, naturally occurring anti-oxidant, sometimes referred to as the "universal anti-oxidant" because of its activity and solubility in both water and lipids. ALA is able to penetrate into skin cells, is able to prevent activation of the proinflammatory NF-kB pathway responsible for breakdown of collagen and elastin, and is able to boost the protective effects of vitamins E and C, thereby boosting naturally occurring anti-oxidants within cells.

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[0064] In one embodiment, tetrahexyldecyl ascorbate may be incorporated in the composition of the present invention. Tetrahexyldecyl ascorbate is a stable, lipid-soluble ester derivative of vitamin C. Vitamin C has been reported to promote collagen synthesis, inhibit lipid breakdown, regenerate vitamin E, reduce fine lines and wrinkles, heal sunburns, and is a potent anti-oxidant scavenger of free radicals having significant anti-inflammatory properties, hindering production of e.g., arachidonic acid.

[0065] In another embodiment, panthenol or its equivalents are contemplated for use with this invention. Panthenol is an effective film-forming moisturizing agent having anti-inflammatory properties. Panthenol equivalents may include alcohol derivatives of pantothenic acid, such as the ones described in CTFA Cosmetic Ingredient Handbook, The Cosmetic, Toiletry and Fragrance Association, Inc., pp. 272-273, 1992. For optimal usefulness, the amount of panthenol should be chosen so that the composition dries reasonably quickly. The more panthenol in the composition, the longer it takes for the composition to dry when it is applied to skin or other surfaces.

[0066] Vitamins, minerals, and/or anti-oxidants may be present in a collective amount ranging from about 0.01 % to 20 % by weight of the total composition, desirably from about 0.1 wt % to about wt 10 %, more desirably from about 0.5 wt % to about 3 wt %.

[0067] Optionally, the present composition may additionally include one or more anesthetics, anti-allergens, anti-irritants, antifungals, anti-microbials, anti-inflammatory agents, antiseptics, chelating agents, colorants, depigmenting agents, emollients, emulsifiers, film formers, fragrances, humectants, insect repellents, lubricants, moisturizers, pharmaceutical agents, photostabilizing agents, preservatives, skin protectants, skin penetration enhancers, sunscreens, stabilizers, surfactants, thickeners, viscosity modifiers, or any combinations thereof.

[0068] The present invention provides plant or botanical ingredients and natural, active ingredients having anti-irritant or anti-inflammatory properties to counter potential irritation to skin. Although some embodiments lack the use of exfoliating agents, these agents may be included provided that sufficient anti-irritant/anti-inflammatory agents are

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included to ameliorate the irritating effects of exfoliating agents. Exemplary anti-irritants include, but are not limited to, aloe vera, α -bisabolol, caffeine or other xanthenes, chamomile, cola nitada extract, dipotassium glycyrrhizinate, glycyrrhizic acid and its derivatives, green tea extract, lecithin or hydrogenated lecithin, licorice extract, tea tree oil, steroidal or non-steroidal anti-inflammatory agents, including, but not limited to cyclooxygenase inhibitors (e.g., salicylic acid, acetylsalicylic acid), NF- κ B inhibitors, strontium acetate, strontium chloride, strontium nitrate, urea, or combinations thereof. Desirable anti-irritants may include dipotassium glycyrrhizinate, lecithin and hydrogenated lecithin.

[0069] Anti-irritant or anti-inflammatory agents may be present individually or collectively in an amount ranging from about 0.01 % to 10 % by weight of the total composition, desirably from about 0.05 wt % to about wt 5 %, more desirably from about 0.2 wt % to about 1.5 wt %.

[0070] The plant ingredients, plant extracts, oils, vitamins, minerals, antioxidants, anti-irritants or other active agents may be included, either individually or collectively, in a pharmaceutically or cosmetically acceptable vehicle. Examples of pharmaceutically or cosmetically acceptable vehicles suitable for the embodiments of the present invention include, but are not limited to, water, C1-C4 alcohols, fatty alcohols, fatty ethers, fatty esters, glycerin, glycols, vegetable oils, mineral oils, lecithin, hydrogenated lecithin, liposomes, laminar lipid materials, phospholipids, polyglycols, polyols, propyl alcohol, silicone oils, vegetable oil, or any combinations thereof.

[0071] The pharmaceutically or cosmetically acceptable vehicle of the present invention may be in the form of a homogeneous phase formulation or in the form of an emulsion or microemulsion including, but not limited to, oil-in-water, water-in-oil and multiple including triple, phase emulsions. These emulsions can cover a broad range of consistencies including thin lotions (which can also be suitable for spray or aerosol delivery), creamy lotions, light creams and heavy creams. Other suitable topical carriers include anhydrous liquid solvents such as oil and alcohol; aqueous-based single phase liquid solvent (e.g., hydro-alcoholic solvent system); anhydrous solid and semisolid (such as gel and stick); and aqueous based gel and mousse system.

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[0072] The pharmaceutically or cosmetically acceptable vehicle will usually contain from about 5% to about 99.9% by weight of the total composition, desirably from about 25% to about 80%, and more desirably from about 50% to about 70% by weight of the composition, and may, in the absence of other cosmetic adjuncts, form the balance of the composition.

[0073] Emollients are moisturizers to maintain hydration or to rehydrate the skin by providing a protective emollient coating. Emollients may be classified under such general chemical categories as esters, fatty acids and alcohols, polyols and hydrocarbons. Esters may be mono- or di-esters. Representative examples of fatty di-esters include, but are not limited to, dipotassium glycyrrhizinate, dibutyl adipate, diethyl sebacate, diisopropyl dimerate, and dioctyl succinate. Acceptable branched chain fatty esters include, but are not limited to, 2-ethyl-hexyl myristate, isopropyl stearate and isostearyl palmitate. Acceptable tribasic acid esters include, but are not limited to, triisopropyl trilinoleate and triauryl citrate. Acceptable straight chain fatty esters include, but are not limited to, lauryl palmitate, myristyl lactate, and stearyl oleate.

[0074] Suitable fatty alcohols and acids may include, but are not limited to, alcohols or acids having from about 10 to 20 carbon atoms. For example, alcohols such as cetyl, myristyl, palmitic and stearyl alcohols and acids may be used.

[0075] Polyols may serve as emollients, including, but not limited to linear and branched chain alkyl polyhydroxyl compounds. Representative polyols, include, but are not limited to butylene, propylene glycol, sorbitol, glycerin, polymeric polyols, such as polypropylene glycol and polyethylene glycol, and the like.

[0076] Hydrocarbons may serve as emollients and may include hydrocarbon chains having from about 12 to 30 carbon atoms, including, but not limited to mineral oil, petroleum jelly, squalene and isoparaffins.

[0077] Exemplary emollients include, but are not limited to, butylene, caprylic/capric triglycerides, castor oil, ceteareth-20, ceteareth-30, cetearyl alcohol, ceteth 20, cetostearyl alcohol, cetyl alcohol, cetyl stearyl alcohol, cholesterol, cocoa butter, diisopropyl adipate, glycerin, glyceryl monooleate, glyceryl monostearate, glyceryl

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stearate, isoparaffins, isopropyl myristate, isopropyl palmitate, lanolin, lanolin alcohol, hydrogenated lanolin, isoparaffins, liquid paraffins, linoleic acid, mineral oil, oleic acid, petroleum jelly, phospholipids, polyethylene glycol, polyethylene glycol-7 glyceryl cocoate, polyethylene glycol-18 methyl ester dimethyl silane, polyoxyethylene glycol fatty alcohol ethers, polyoxypropylene 15-stearyl ether, polypropylene glycol propylene glycol, propylene glycol stearate, sorbitol, sphingolipids, squalene, steareth-2 or -100, stearic acid, stearyl alcohol, urea, white petrolatum, and the like.

[0078] Emollients may be present individually or collectively in an amount ranging from about 0.005 % to 20 % by weight of the total composition, desirably from about 0.1 wt % to about wt 10 %, more desirably from about 1.0 wt % to about 5.0 wt %.

[0079] Humectants are moisturizers that can bind water and retain it on the skin surface. Exemplary humectants include, but are not limited to, acetyl glucosamine, bisaccharide gum, butylene glycol, ethoxydiglycol, ethylene glycol/polypropylene, glucose, glycereth-26, glycerin, glycerol, glycol, lactitol, maltitol, propylene glycol, sericin, sodium hyaluronate, sorbitol, xylitol, sodium citrate, glucose and the like.

[0080] Humectants may be collectively present in an amount ranging from about 0.1 % to 40 % by weight of the total composition, desirably from about 2.5 wt % to about wt 25 %, more desirably from about 5 wt % to about 15 wt %.

[0081] The present compositions may provide one or more preservatives. Suitable preservatives include disodium EDTA, benzyl alcohol, methylparaben, phenoxyethanol, propylparaben, ethylparaben, butylparaben and isobutylparaben.

[0082] Another category of functional ingredients within the cosmetic compositions of the present invention are thickeners. Thickeners will usually be present in a collective amount ranging anywhere from about 0.01 to 10 % by weight, desirably from about 0.05 to 5 % by weight, more desirably from about 0.1 % to 1 % by weight of the composition. Exemplary thickeners are cross-linked polyacrylate materials. Gums such as xanthan, carrageenan, gelatin, karaya, pectin and locust bean gum may be used. Under certain circumstances the thickening function may be accomplished by a material also serving

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as a silicone or emollient. For instance, silicone gums in excess of 10 centistokes and esters such as glycerol stearate have dual functionality.

[0083] Powders may be incorporated into the cosmetic composition of the invention. These powders include chalk, talc, kaolin, starch, smectite clays, chemically modified magnesium aluminum silicate, organically modified montmorillonite clay, hydrated aluminum silicate, fumed silica, aluminum starch octenyl succinate and mixtures thereof.

[0084] Other adjunct minor components may also be incorporated into the cosmetic compositions. These ingredients may include coloring agents, opacifiers and perfumes. Amounts of these other adjunct minor components may range anywhere from 0.001% up to 20% by weight of the composition.

[0085] The compositions of the present invention may be formulated in any convenient form suitable for topical application to the skin. Such product forms include, but are not limited to, aerosol spray, cream, dispersion, emulsion, foam, gel, liquid, lotion, mousse, ointment, patch, pomade, powder, pump spray, solid, solution, stick, and towelette. A desired cosmetic form is a cream that is an oil-in-water emulsion. Water-in-oil and water-in-silicone emulsions also are contemplated.

[0086] The composition can be packaged in a suitable container to suit its viscosity and intended use by the consumer. For example, a lotion or a cream can be packaged in a bottle or a roll-ball applicator, or a propellant-driven aerosol device or a container fitted with a pump suitable for finger operation. When the composition is a cream, it can simply be stored in a non-deformable bottle or squeeze container, such as a tube or a lidded jar. The invention accordingly also provides a closed container containing a cosmetically acceptable composition as herein defined.

[0087] The present invention also contemplates a kit suitable for a treatment regime to provide an amount of the cosmetic composition suitable for a desired period of time, such as fourteen days. According to this embodiment, the kit includes a package that contains a plurality of containers, with each container having an amount of the cosmetic

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composition according to the present invention suitable for a single use. The container may be in the form of a vial or other suitable holding device.

[0088] In one embodiment, the kit includes a package having a plurality of vials, each vial containing a sufficient amount of the cosmetic composition of the present invention suitable for a single application of the cosmetic composition to the skin. The kit may be formulated to provide a number of vials matching the number of days in which the cosmetic composition is applied to skin. Alternatively, the kit may be formulated for more than one application per day. In one embodiment, the kit may contain 14 vials for daily treatment to skin over a period of 14 days. The kit may further contain one or more applicators for applying the compositions and may further include a set of instructions for use of the kit.

[0089] The present invention also includes methods of treating skin by topically applying the cosmetic compositions of the present invention. In use, a small quantity of the composition, for example from 1 to 100 ml, may be applied to exposed areas of the skin, from a suitable container or applicator and, if necessary, it is then spread over and/or rubbed into the skin using the hand or fingers or a suitable device.

[0090] In one embodiment, the present invention provides a method for preventing, arresting, reversing, ameliorating, diminishing, reducing or improving a sign of aging, in which a composition of the present invention is topically applied to skin in a cosmetically effective amount sufficient to prevent, arrest, reverse ameliorate, diminish, reduce or improve a sign of aging in skin. Exemplary signs of aging include, but are not limited to, facial lines, fine lines, wrinkles, crow's feet, dark eye circles, blemishes, age spots, stretch marks, or combinations thereof.

[0091] In another embodiment, the present invention provides a method for improving the aesthetic appearance of skin, in which a composition of the present invention is topically applied to skin in a cosmetically effective amount sufficient to improve the aesthetic appearance of the skin. The improvements may relate to skin thickness, elasticity, resiliency, moisturization, tone, texture, radiance, luster, brightness,

clarity, contour, firmness, tautness, suppleness, softness, sensitivity, pore size, or combinations thereof.

[0092] The improvements may further relate to improving adverse skin conditions affected by, resulting in or resulting from the group consisting of psoriasis, eczema, seborrhea, dermatitis, sunburn, estrogen imbalance, hyperpigmentation, hypopigmentation, discoloration, yellowing, freckles, skin atrophy, skin breakout, skin fragility, dryness, chapping, sagging, thinning, hyperplasia, fibrosis, enlarged pores, cellulite formation, bruising, acne formation, apoptosis, cellular differentiation, cellular de-differentiation, prevention of tumor induction or tumor progression, viral infections, fungal infections, bacterial infections, spider veins (telangiectasia), hirsutism, rosacea, pruritis, calluses, warts, corns, or combinations thereof.

[0093] The signs of aging or adverse skin conditions may result from free radical damage, environmental agents, pollutants, diet, chronological aging, premature aging, hormonal aging, photo-aging, or combinations thereof. Accordingly, the present compositions and methods selected for improved anti-aging characteristics or adverse skin conditions may employ topical application of active ingredients inhibiting enzymes or mediators that accelerate or facilitate aging, damage, formation of free radicals, or breakdown of skin elements, including, but not limited to metalloproteinases, collagenases, elastases, hyaluronidases, and proteases. The active ingredients may have anti-oxidant activity, free radical scavenging or anti-inflammatory activity and/or they may inhibit breakdown of collagen, elastin, fibronectin, hyaluronic acid, glycosaminoglycans (GAG) or other extracellular matrix elements or regulatory enzymes or mediators of the NF- κ B signal transduction pathway. The active agents may also inhibit other signal transduction pathways associated with aging, including the mediators and regulators associated with these pathways, or combinations thereof.

[0094] In addition to improving the aesthetic or cosmetic appearance of skin, the topical compositions of the present invention may be topically applied to enhance the general health, vitality and appearance of the skin. For example, the present composition may be applied to skin to improve microcirculation, communication among

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skin cells, replenishment of essential nutrients or skin constituents, or to improve the metabolism, proliferation, multiplication, turnover and/or exfoliation of skin cells.

[0095] Exfoliation may be carried out with or without the use of alpha- or beta hydroxy acids or other exfoliants, or combinations thereof by topical application to skin. When using exfoliating agents in the compositions of the present invention, sufficient anti-irritant or anti-inflammatory agents are included to neutralize the potential irritation associated with exfoliating agents in the absence of such neutralizing agents.

[0096] The following are non-limiting examples of the present invention. Unless indicated otherwise, all proportions and percentages are by weight.

[0097] EXAMPLE 1

[0098] The following are examples of formulations according to the present invention.

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[0099]

TABLE 1

Ingredients	Amount (percent)
Rosemary leaf extract	0.01-0.5
Centella asiatica extract	0.01-0.08
Echinacea angustifolia extract	0.005-0.02
Alpinia speciosa leaf extract	0.01-0.08
Ultrasones™	0.05-3.0
Other plant ingredients	0.1-2.0
Vitamins	0.1-3.0
Preservatives	0.5-2.0
Humectants	10.0-25.0
Anti-Irritants	0.2-1.5
pH Adjuster	0.2-1.0
Thickener	0.05-1.5
Emollient	1.0-5.0
Water	q.s.

The formulation shown in Table 1 may be provided in small quantities and applied directly to the face over a periodic basis.

TABLE 2

Ingredients	Amount (percent)
Rosemary leaf extract	0.01-5.0
Alpinia speciosa leaf extract	0.01-5.0
Ultrasones™	0.05-3.0
Other plant ingredients	0.1-2.0
Vitamins	0.1-3.0
Preservatives	0.5-2.0
Humectants	10.0-25.0
Anti-Irritants	0.2-1.5
pH Adjuster	0.2-1.0
Thickener	0.05-1.5
Emollient	1.0-5.0
Water	q.s.

The formulation shown in Table 2 may be provided in small quantities in a patch and applied under the eyes over a periodic basis

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EXAMPLE 2

[00100] The composition of Table 1 in Example 1 was tested in the following manner. Females between the age of 35 and 70, who were currently using a facial regimen consisting of a cleanser, toner and moisturizer twice-daily, who perceived themselves as having normal-to-dry or dry facial skin, and who had mild to moderate fine lines in the left periorcular area (as determined by clinical grading) were chosen as test subjects. The test subjects were to continue use of their regular brands of skin care products, to not begin use of new skin or hair care products, and to avoid sun exposure (including tanning beds) and swimming pools for the duration of the study.

[00101] The test subjects were to use their normal facial skin care regimen (cleanser, toner and moisturizer twice-daily) and then to apply the composition of Table 1 of Example 1 after use of the toner and prior to the use of the moisturizer. The subjects were to use the composition daily for fourteen days and to be clinically evaluated at the start (day 1) and on days 4, 7, 10, and 14. During each evaluation, the clinician evaluated the skin for (1) the presence of mild to moderate fine lines, (2) tactile roughness, (3) clarity, (4) dryness/scaling. Each attribute was grading according to the following scale:

[00102] Fine lines (0=none and 10=severe)

[00103] Tactile Roughness (0=smooth and 10=rough)

[00104] Clarity (0=dull, matte appearance and 10=bright, luminous appearance)

[00105] Dryness/scaling (0=moist and 10=severe dryness).

[00106] In addition, corneometer measurements were taken to evaluate the moisture content in the left cheek skin at Baseline and at Days 4, 7, 10 and 14. The corneometer (CM 825) was placed on the cheek, in line with the center of the eye, on the ocular bone. Triplicate measurements were taken. The corneometer quantifies moisture content in the stratum corneum (SC) by an electrical capacitance method. The measurement has no units, but is proportional to the dielectric constant of the surface

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layers of the skin, and increases as the skin becomes more hydrated. The readings are directly related to the skin's electrical capacitance (picoFarads).

[00107] FIG. 1a shows the reduction in fine lines over a 14 day period during which a composition of Example 1 was applied daily to 62 test subjects. The y-axis depicts mean score changes for the 62 test subjects at the time of evaluation (at Baseline and at Days 4, 7, 10 and 14). As reflected in FIG. 1a, the Day 14 score represented a scoring change of -4.8 relative to the Baseline score. FIG. 1b is a graph that depicts the % improvement in fine lines expressed in % reduction in fine lines over the 14 day period during which a composition of Example 1 was applied daily. The graph illustrates a >70% reduction in fine lines by Day 4 and a 99% reduction in fine lines by Day 14.

[00108] FIG. 2a shows the reduction in skin tactile roughness over a 14 day period during which a composition of Example 1 was applied daily. The y-axis depicts the change in scores between the Baseline and Days 4, 7, 10 and 14 (Baseline score minus score upon evaluation). As reflected in FIG. 2a, the Day 14 score represented a scoring change of -0.85 relative to the Baseline score. FIG. 2b is a graph that depicts the % improvement in skin smoothness expressed in % reduction in skin tactile roughness over the 14 day period during which a composition of Example 1 was applied daily. The graph illustrates a >50% reduction in tactile roughness by Day 4 and a >80% reduction by Days 10-14.

[00109] FIG. 3a shows the increase in skin clarity over a 14 day period during which a composition of Example 1 was applied daily. The y-axis depicts the change in scores between the Baseline and Days 4, 7, 10 and 14 (Baseline score minus score upon evaluation). As reflected in FIG. 3a, the Day 14 score represented a scoring change of 2.91 relative to a Baseline score. FIG. 3b is a graph that depicts the % improvement in skin clarity expressed in % increase in skin clarity over the 14 day period during which a composition of Example 1 was applied daily. The graph illustrates a >150% increase in skin clarity by Day 4, and >250% increase in skin clarity by Day 14.

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[00110] FIG. 4a shows the reduction in skin dryness over a 14 day period during which a composition of Example 1 was applied daily. The y-axis depicts the change in scores between the Baseline and Days 4, 7, 10 and 14 (Baseline score minus score upon evaluation). As reflected in FIG. 4, the Day 14 score of 0.06 represented a scoring change of -4.50 relative to the Baseline score. FIG. 4b is a graph that depicts the % improvement in skin dryness expressed in % reduction in skin dryness over the 14 day period during which a composition of Example 1 was applied daily. The graph illustrates a >90% reduction in fine lines by Day 4 and a 99% reduction in fine lines by Day 14.

[00111] FIG. 5a shows the increase in skin moisture content over a 14 day period during which a composition of Example 1 was applied daily. The y-axis depicts the change in scores between the Baseline and Days 4, 7, 10 and 14 (Baseline score minus score upon evaluation). As reflected in FIG. 5a, the Day 14 score represented a scoring change of 10.04 relative to the Baseline score. FIG. 5b is a graph depicting % moisturization when a representative composition of the present invention was topically applied to the skin over a 14 day period.

[00112] FIG. 6a shows the increase in skin moisture content over a 12 hour period in which a composition of Example 1 was applied immediately following Baseline measurements. The y-axis depicts the change in score between the Baseline (i.e., initial) and the 4, 8, and 12 hour measurements. FIG. 6b is a graph depicting the % improvement in skin moisture content expressed in % improvement in moisturization over a 12 hour period during which a composition of Example 1 was applied immediately following Baseline measurements. This graph illustrates a greater than 25% increase in moisturization after 12 hours.

[00113] FIG. 7a is a photograph of a portion of a subject's face before daily application of the composition of Table 1 of Example 1. FIG. 7b is a photograph of a portion of the subject's face after daily application of a composition of Table 1 of Example 1 over a period of fourteen days. It can be seen that application of the composition of Table 1 of Example 1 resulted in a reduction in fine lines.

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[00114] FIG. 8a is a photograph of a portion of another subject's face before application of the before daily application of the composition of Table 1 of Example 1. FIG. 8b is a photograph of a portion of the subject's face after daily application of a composition of Table 1 of Example 1 over a period of fourteen days. It can be seen that application of the composition of Example 1 again resulted in a reduction in fine lines.

[00115] While the invention has been described in conjunction with specific embodiments, it is to be understood that many alternatives, modifications, and variations will be apparent to those skilled in the art in light of the foregoing description. Accordingly, this invention is intended to embrace all such alternatives, modifications, and variations that fall within the spirit and scope of the appended claims.

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133**CLAIMS**

1. A topical composition comprising:
 - a. at least one plant ingredient or plant extract from *Rosmarinus officinalis*;
 - b. at least one plant ingredient or plant extract from *Centella*, *Echinacea* or *Alpinia*;
 - c. at least one DNA repair enzyme; and
 - d. at least one pharmaceutically or cosmetically acceptable vehicle.
2. The composition of claim 1, where the at least one plant ingredient from *Rosmarinus officinalis* includes a member of the group consisting of ursolic acid, carnosic acid, rosmarinic acid, and oleanolic acid.
3. The composition of claim 1, comprising at least one *Rosmarinus officinalis* plant extract.
4. The composition of claim 3, where the at least one *Rosmarinus officinalis* plant extract is present in an amount from about 0.001 to about 10% by weight of the total composition.
5. The composition of any of claims 1-4, comprising at least one *Centella* plant extract.
6. The composition of any of claims 1-4, comprising a *Centella asiatica* plant extract
7. The composition of any of claims 1-4, comprising at least one *Centella* plant extract present in an amount from about 0.001 to about 10% by weight of the total composition.

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8. The composition of any of claims 1-4, comprising at least one *Echinacea* plant ingredient or plant extract.
9. The composition of any of claims 1-4, comprising at least one *Echinacea* plant ingredient or plant extract is from a member of the group consisting of *E. purpurea*, *E. angustifolia*, and *E. pallida*.
10. The composition of any of claims 1-4, comprising at least one *Echinacea* plant extract is present in an amount from about 0.0001 to about 1% by weight of the total composition.
11. The composition of any of claims 1-4, comprising at least one *Alpinia* plant ingredient.
12. The composition of any of claims 1-4, comprising at least one *Alpinia* plant extract.
13. The composition of any of claims 1-4, comprising an *Alpinia speciosa* plant extract.
14. The composition of any of claims 1-4, comprising at least one *Alpinia* plant extract is present in an amount from about 0.001 to about 10% by weight of the total composition.
15. The composition of claim 1, comprising plant ingredients or plant extracts selected from at least two members of the group consisting of *Centella asiatica*, *Echinacea angustifolia*, and *Alpinia speciosa*.
16. The composition of claim 1, comprising plant ingredients or plant extracts from each member of the group consisting of *Centella asiatica*, *Echinacea angustifolia*, and *Alpinia speciosa*.

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17. The composition of claim 1, 15, or 16, where the at least one DNA repair enzyme is a pyrimidine glycosylase/abasic lyase.

18. The composition of claim 1, 15, or 16, where the at least one DNA repair enzyme is selected from the group consisting of bacteriophage T4 pyrimidine dimer-specific endonuclease, *Micrococcus luteus* N-glycosylase/AP lyase, *Saccharomyces cerevisiae* N-glycosylase/apurinic-apyrimidinic lyase, *Schizosaccharomyces pombe* UV damage endonuclease (UVDE), *Chlorella virus* isolate PBCV-1 pyrimidine dimer-specific glycosylase, and *Anacystis nidulans* photolyase.

19. The composition of claim 1, 15, or 16, further comprising at least one vitamin selected from the group consisting of vitamin A, vitamin B3, vitamin B5, vitamin C, and vitamin E.

20. The composition of claim 1, 15, or 16, further comprising tetrahexyldecyl ascorbate or ascorbyl palmitate.

21. The composition of claim 1, 15, or 16, further comprising at least one plant or botanical extract or oil selected from the group consisting of *Ricinus communis* (castor) oil, *Glycyrrhiza glabra* (licorice) root extract, hydrolyzed oats, *Citrus medica limonum* (lemon) extract, *Cucumis sativus* (cucumber) extract, and *Helianthus annus* (sunflower) extract.

22. The composition of claim 1, 15, or 16, comprising *Ricinus communis* (castor) oil, *Glycyrrhiza glabra* (licorice) root extract, hydrolyzed oat proteins, *Citrus medica limonum* (lemon) extract, *Cucumis sativus* (cucumber) extract, and *Helianthus annus* (sunflower) extract.

23. The composition of claim 1, 15, or 16, where the at least one vehicle includes one or more ingredients selected from the group consisting of water, glycerin, C1-C4

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alcohols, fatty alcohols, fatty ethers, fatty esters, polyols, glycols, vegetable oils, mineral oils, liposomes, laminar lipid materials, silicone oils, and combinations thereof.

24. The composition of claim 1, 15, or 16, where the composition is in a product form selected from the group consisting of aerosol, cream, emulsion, solid, liquid, dispersion, foam, gel, lotion, mousse, ointment, powder, patch, pomade, solution, pump spray, stick, towelette, and combinations thereof.

25. The composition of claim 1, 15, or 16, where the at least one pharmaceutically or cosmetically acceptable vehicle is a liposome.

26. The composition of claim 1, 15, or 16, where the at least one pharmaceutically or cosmetically acceptable vehicle is a liposome that encapsulates at least one plant ingredient or plant extract from *Rosmarinus officinalis*.

27. The composition of claim 1, 15, or 16, where the at least one pharmaceutically or cosmetically acceptable vehicle is a liposome that encapsulates at least one plant ingredient or plant extract from *Centella*, *Echinacea* or *Alpinia*.

28. The composition of claim 1, 15, or 16, where the at least one pharmaceutically or cosmetically acceptable vehicle is a liposome that encapsulates at least one DNA repair enzyme.

29. The composition of claim 1, 15, or 16, where the at least one pharmaceutically or cosmetically acceptable vehicle is a liposome that encapsulates *Micrococcus luteus* N-glycosylase/AP lyase.

30. The composition of claim 1, 15, or 16, where the liposome-encapsulated DNA repair enzyme is present in an amount from about 0.05 % to about 5% by weight of the total composition.

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31. The composition of claim 1, 15, or 16, where the liposome encapsulates at least one vitamin selected from the group consisting of vitamin A, vitamin B3, vitamin B5, vitamin C, vitamin E, and derivatives thereof.

32. The composition of claim 1, 15, or 16, where the liposome encapsulates at least one member selected from the group consisting of *Ricinus communis* (castor) oil, *Glycyrrhiza glabra* (licorice) root extract, hydrolyzed oats, *Citrus medica limonum* (lemon) extract, *Cucumis sativus* (cucumber) extract, and *Helianthus annuus* (sunflower) extract.

33. A topical composition comprising:

- a. a plant extract from *Rosmarinus officinalis*, *Centella asiatica*, *Echinacea angustifolia*, and *Alpinia speciosa*;
- b. a liposome-encapsulated *Micrococcus luteus* N-glycosylase/AP lyase; and
- c. at least one pharmaceutically or cosmetically acceptable vehicle.

34. A topical composition comprising:

- a. a plant extract from *Rosmarinus officinalis* and *Alpinia speciosa*;
- b. a liposome-encapsulated *Micrococcus luteus* N-glycosylase/AP lyase; and
- c. at least one pharmaceutically or cosmetically acceptable vehicle.

35. A method of improving at least one sign of aging in skin, comprising topically applying to the skin the composition of claim 1, in a cosmetically effective amount sufficient to improve at least one sign of aging in skin.

36. The method of claim 35, where the at least one sign of aging is selected from the group consisting of lines, fine lines, wrinkles, crow's feet, dark eye circles, blemishes, age spots, and stretch marks.

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37. The method of claim 35, where the at least one sign of aging results from at least one of free radical damage, environmental agents, pollutants, diet, chronological aging, premature aging, hormonal aging, and photo-aging.

38. A method of improving the appearance of skin, comprising topically applying to the skin the composition of claim 1 in a cosmetically effective amount sufficient to improve the appearance of the skin.

39. The method of claim 38, where the improvement is selected from the group consisting of skin thickness, elasticity, resiliency, moisturization, smoothness, tone, texture, radiance, luster, brightness, clarity, contour, firmness, tautness, suppleness, softness, sensitivity, pore size, and combinations thereof.

40. The method of claim 38, where the improvement is directed to at least one adverse skin condition selected from the group consisting of psoriasis, eczema, seborrhea, dermatitis, sunburn, estrogen imbalance, hyperpigmentation, hypopigmentation, discoloration, yellowing, freckles, skin atrophy, skin breakout, skin fragility, dryness, tactile roughness, chapping, sagginess, thinning, hyperplasia, fibrosis, enlarged pores, cellulite formation, bruising, acne formation, apoptosis, cellular differentiation, cellular de-differentiation, prevention of tumor induction or tumor progression, viral infections, fungal infections, bacterial infections, spider veins (telangiectasia), hirsutism, rosacea, pruritis, calluses, warts, corns, and combinations thereof.

41. A kit for improving the appearance of skin comprising:

- a. at least one container containing the composition of claim 1; and,
- b. instructions for applying the composition from said at least one container.

42. The kit of claim 41, comprising a plurality of containers.

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FIGURE 1a

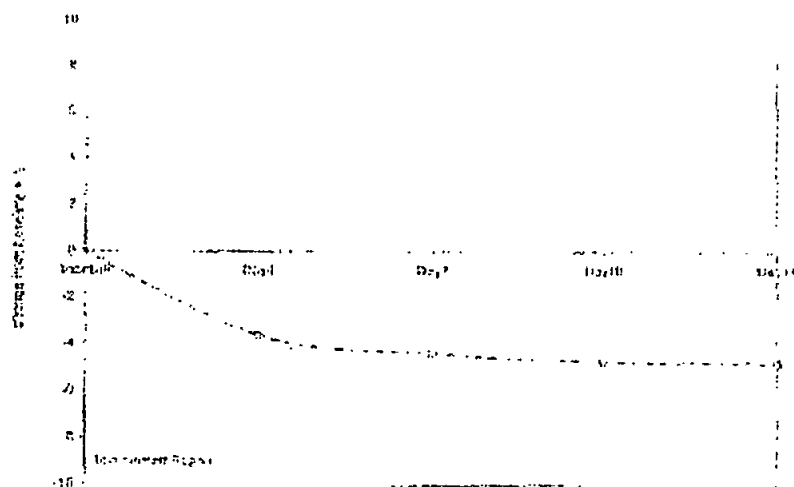
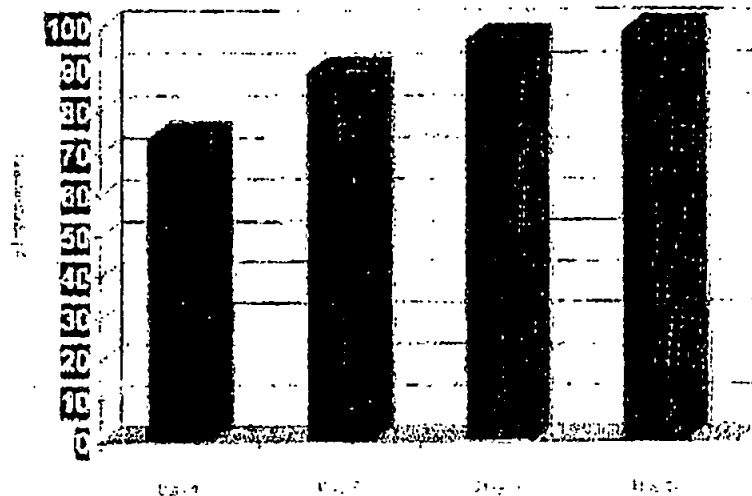


FIGURE 1b



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FIGURE 2a

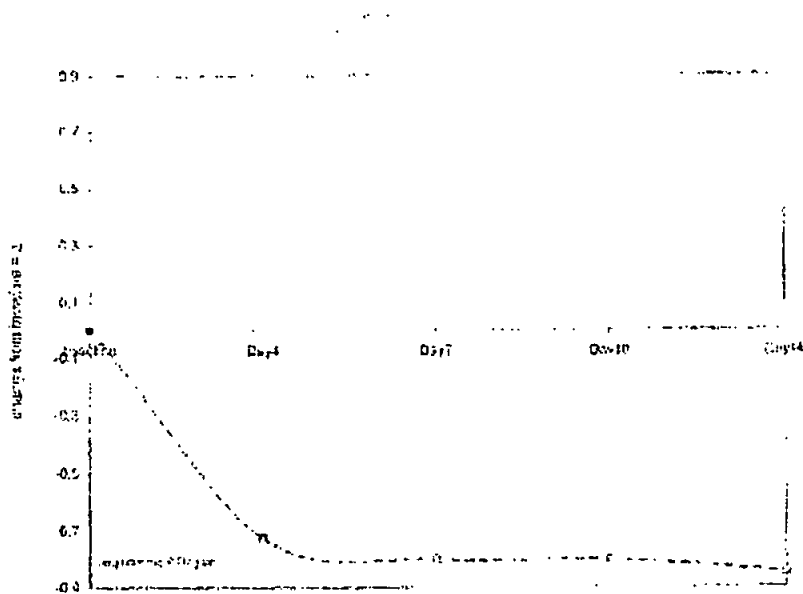
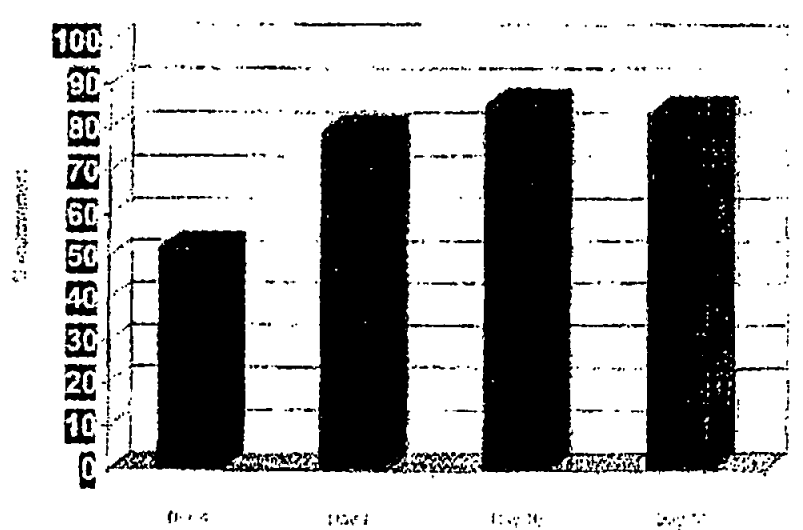


FIGURE 2b



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FIGURE 3a

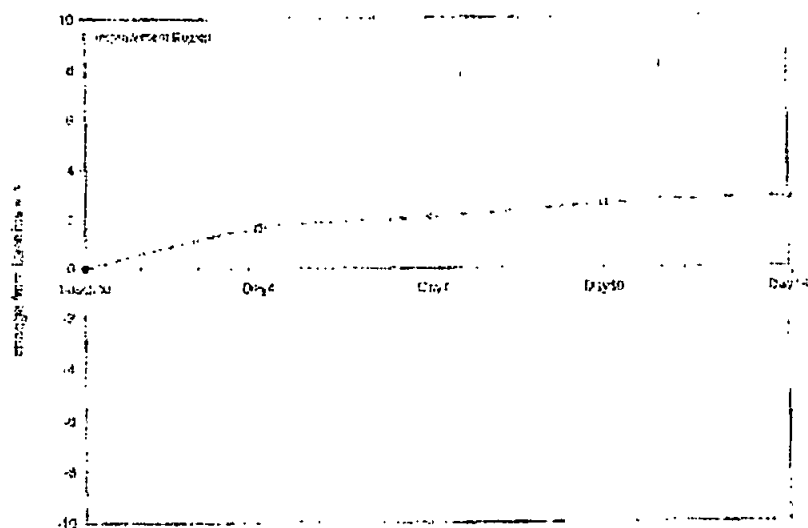
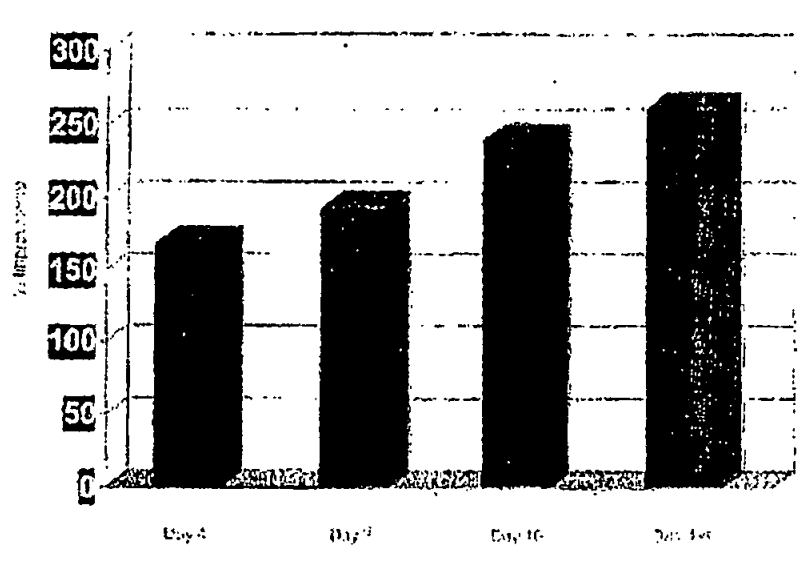


FIGURE 3b



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FIGURE 4a

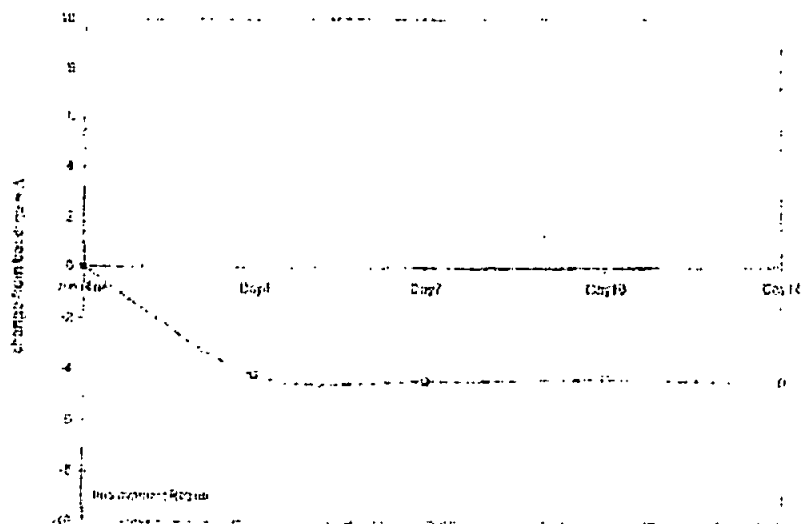
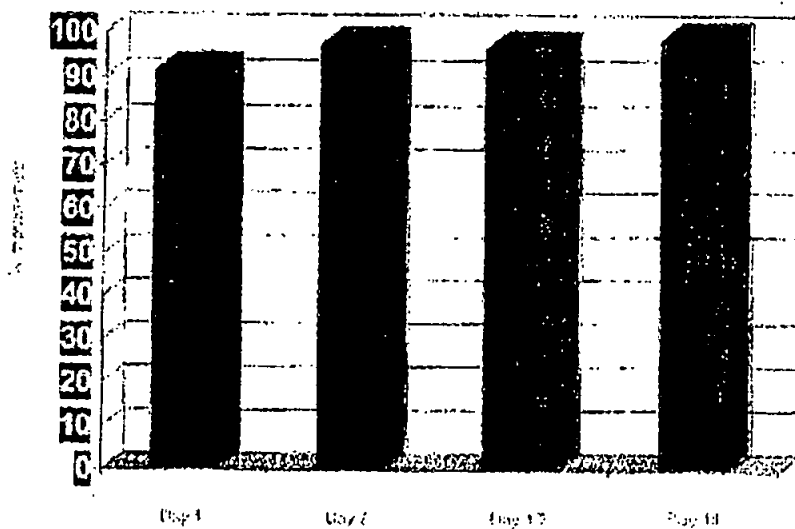


FIGURE 4b



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FIGURE 5a

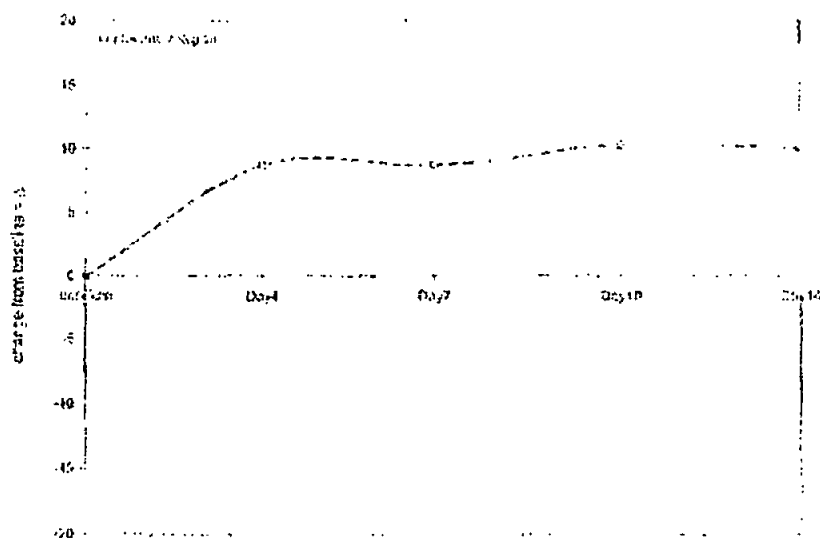
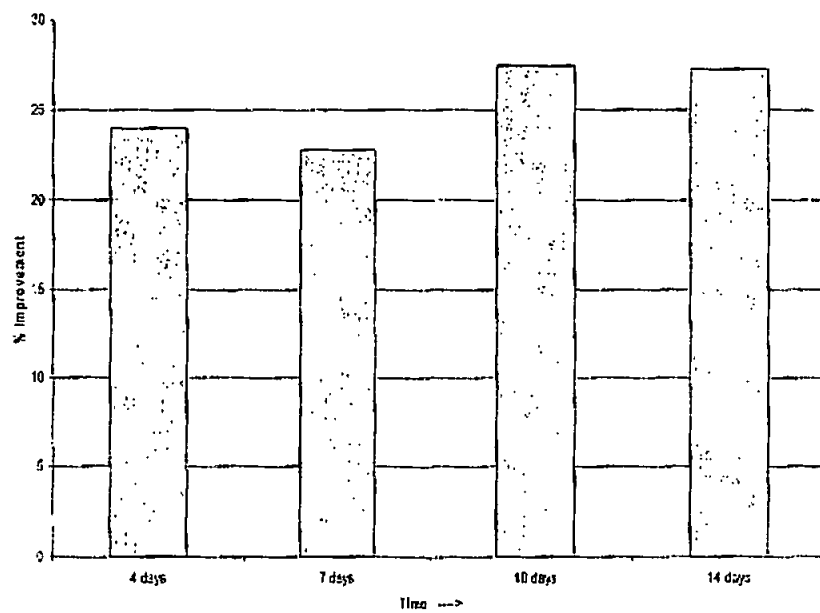


FIGURE 5b



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FIGURE 6a

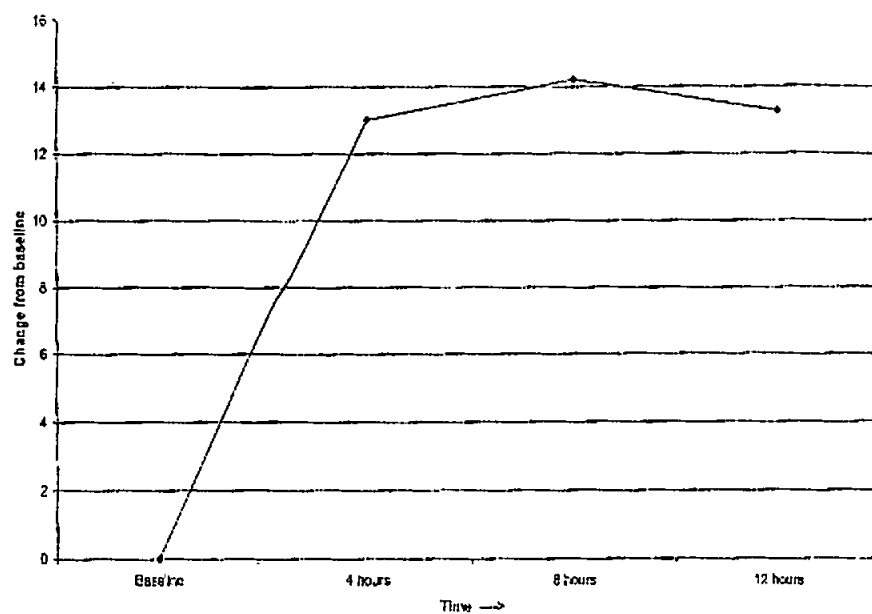
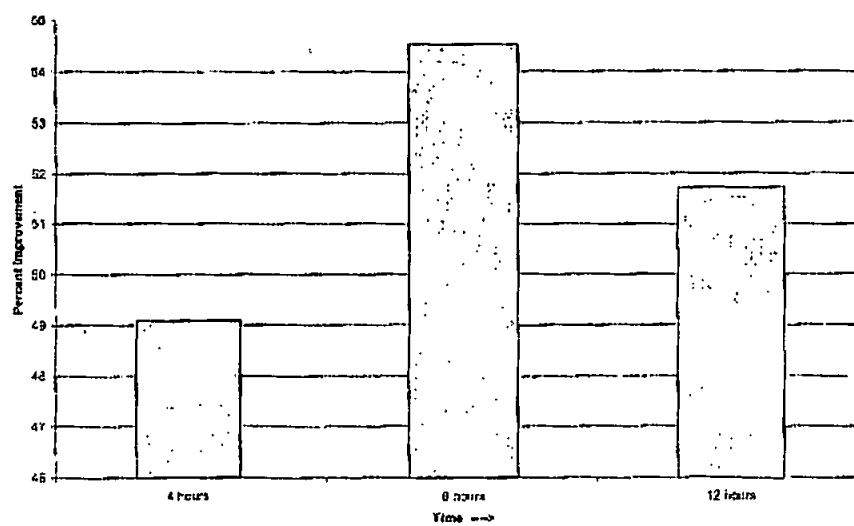


FIGURE 6b



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FIGURE 7a



FIGURE 7b



FIGURE 8a



FIGURE 8b



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2020
Bogotá, D.C.,

Doctor:
Jaime Eduardo Delgado Villegas
Apoderado

Oficio N°:

-2- 12489

ASUNTO:

Radicación PCT N°	08-46044
Trámite	011
Evento	379
Actuación	440
Folios	008

Con fundamento en lo previsto por el artículo 43 de la Decisión 486 de la Comisión de la Comunidad Andina, se le comunica que la oposición presentada por la doctora Cielo Ángela Peña Rodríguez, en su calidad de apoderada de Gynopharm S.A., reúne los requisitos formales exigidos por la ley al momento de su presentación.

En cumplimiento de lo dispuesto en la citada norma, se le concede el término de sesenta (60) días hábiles siguientes a la fecha de notificación del presente oficio, para que haga valer sus argumentaciones y presente pruebas.

Notifíquese el presente oficio conforme a lo dispuesto en el numeral 5.2, literal e), del capítulo quinto del título primero de la Circular Única N° 10 de 2001.


ALIX CARMENZA CESPEDES DE VERGEL
Directora de Nuevas Creaciones (C).

El anterior oficio fue notificado por fijación en lista de fecha,

13 NOV. 2009

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