

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
28 December 2006 (28.12.2006)

PCT

(10) International Publication Number
WO 2006/136540 A2

(51) International Patent Classification:

A61K 35/56 (2006.01) A61P 17/00 (2006.01)
A61K 8/98 (2006.01)

(21) International Application Number:

PCT/EP2006/063320

(22) International Filing Date: 19 June 2006 (19.06.2006)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

CL 1511-2005 20 June 2005 (20.06.2005) CL

(71) Applicant (for all designated States except US): **INCUBADORA DE NEGOCIOS GESTA MAYOR, S.A.** [CL/CL]; Av. 11 De Septiembre 2155., Oficina 1203, Providencia, Santiago (CL).

(71) Applicant (for AG only): **BARLOCCI, Anna** [ES/ES]; Balmes, 30 1^ª, E-08007 Barcelona (ES).

(71) Applicant and

(72) Inventor: **MELINAO CANALES, Víctor** [CL/CL]; Av. Américo Vespucio Sur N° 357, Las Condes, Santiago (CL).

(74) Agent: **BARLOCCI, Anna**; Balmes, 30 1^ª, E-08007 Barcelona (ES).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM,

AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))

Published:

- without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: HUMAN SKIN REGENERATING OINTMENT

(57) Abstract: The invention relates to a pharmaceutical or cosmetic composition comprising annelid extracts; to a method for its preparation, and to its use for treating dermatological affections and in surgical or cosmetic treatments. Annelid extract are obtained from earth annelids and/or water annelids. The composition is of natural origin, free of additives; it is useful for treating a series of affections at dermis and epidermis levels, such as: skin affections (injuries, new or old scars, hot water or fire burns, herpes); surgical treatments (scores, tissue repair and healing, skin fortification, pain mitigation, etc.) or cosmetic ones (stimulate pigmentation, acting on antioxidant agents, protection against sun radiation, and others).



WO 2006/136540 A2

Human skin regenerating ointment

FIELD OF INVENTION

The present invention relates to the preparation and use of an easy-to-apply human skin regenerating ointment, the composition of which is of natural origin, free of additives and obtained from earth and/or water annelids. The ointment itself is useful for treating a series of affections at dermis and epidermis levels, such as: skin affections (injuries, new or old scars, hot water or fire burns, herpes); surgical treatments (scores, tissue repair and healing, skin fortification, pain mitigation, etc.) or cosmetologic ones (stimulate pigmentation, acting on anti-oxidant agents, protection against sun radiation, and others).

BACKGROUND OF THE INVENTION

Various products, both of a natural and chemical synthetic origin, are available in the market that are useful to treat, individually, different skin affections, derived from surgical actions, accidents, and others, or to be used for cosmetic purposes, forcing the medical staff, and mainly, patients or those interested to acquire and apply a series of products for the same affection.

There exist independent studies on regenerating-capacity compositions obtained *in vitro* (US 20040063205). Compositions based on natural *Trichuris suis* sources with antibacterial activity, yet not used as a dermatological ointment, have also been described (US 20040029802). Also known are some emulsions of natural origin containing hemoglobin or hemoglobin/myoglobin in the form of cream or lotion for treating poorly oxygenated skin (US 20040022839).

In addition, there are individual studies on the properties of worms wherein they separately use their components to account for specific affections, not for all of them (US 20040063205, US 20040029802, US 20040022839, US 20060047126, US 2005255522, US 20040247603, US 20040147606, US 20040081955). Instead, the present skin regenerating ointment acts at various levels (healing, analgesic, etc) and in a new area, such as skin regeneration.

There is Chilean patent CL 38615 that discloses a natural original cream for

use in cosmetology, which is obtained from snail bave. In addition, Chilean patent application CL 1739-03 discloses a pharmaceutical or cosmetic gel composition comprising snail bave, carbopol, water and preservatives, to treat skin aging, spots, scars, burns, and other affections.

5

There also are commercially available natural origin products for treating skin affections, and some surgical or cosmetologic treatments, such as snail oil (snail-based, Reference: Skin Care Masterpiece), emu oil (base on emu, Reference: EMU Chile S.A), hazelnuts or Rosa Mosqueta oil and/or cream
10 hazelnut and Rosa Mosqueta, Reference: Pharmos Natur (r), Primal Nature Products (r)). Their main characteristics are based on their composition and the properties discovered therein. Thus, emu oil has a high content of linoleic oil, oleic and palmitic oil helping to stimulate new cells, lower or attenuate spots on the skin. Snail cream helps hydration, stopping skin, as
15 Rosa Mosqueta and hazelnut do. However, these products, except for emu oil, generally operate at dermis level.

As for synthetic products, there exist a variety of specific products on the market for each one of the phases of skin affections, surgical or cosmetologic
20 treatments.

Heretofore, no natural origin composition obtained from earth/water annelids has been made for use to treat skin affections.

25 As for the farming of annelids, they have extensively been cultured since antiquity via a technique referred to as Worm Farming for the production of: humus, vermoplast, worm meal as fish feed for salmon farming or treating sewage (Lombriastur M2660557, USPTO 20050090405 USPTO 20040065610, Lombricultura.com, Lombricor.com). However, the species
30 produced to this end is *Eisenia foetida* only, better known as red wiggler.

DESCRIPTION OF THE INVENTION

The present invention relates to the preparation of an easy-to-apply human skin regenerating ointment, the composition of which is 100% natural, since it
35 is an extract of natural organisms, specifically earth and/or water annelids.

According to one aspect, the invention relates to a pharmaceutical or

cosmetic composition comprising annelid extracts.

According to another aspect, the invention relates to a method of preparing a pharmaceutical or cosmetologic composition which comprises the collection
5 of annelids and attainment of the extract from annelids which are the raw material of said composition.

According to a further aspect, the invention relates to the use of the above pharmaceutical composition for the manufacture of a medicament for treating
10 dermatological affections and for surgical or cosmetologic treatments.

The present invention uses a very simple extraction technique, wherein a natural composition is obtained, which is comprised of a number of components characteristic of its source, and this composition is useful to
15 prepare an oil, cream, ointment or powder, useful for treating dermatological affections, surgical or cosmetologic treatments, at dermis and epidermis level.

The pharmacological and/or cosmetic action of this ointment is the result of the different elements comprising this extract.

20 Embodiments of the human skin regenerating ointment are characterized, depending on its composition, in that the base raw materials are earth and/or water annelids, mainly of the *Prosoporus* and *Opistoporus* Family, such as: *Lumbiculida*, of the *Lumbriculidae*, *Branchiobdelidae*, *Acanthobdelodae*,
25 *Alluroididae*, *Sygeonodrilidae*, *Monologastridae*, *Lumbricidae*, *Dorydrilidae* families; being also able to be from the *Monolidastridae*, *haplotaxidae*, *Enchytraeidae*, *Tubificidae*, *Naididae*, *Phreodrilidae*, *Opostocystidae*, *Alluroididae*, *Syngenodrilodae*, *Biwadrolidae*, *Criodrilidae*, *Sparganophilidae*, *Ailoscolecidae*, *Hormogastridae*, *Lumbricidae*, *Lutodrilidae*, *Kynotodae*,
30 *Mocrochaetodae*, *Glossoscolecidae*, *Almidae*, *Onerodrilidae*, *Megascolecidae*, *Eudrilidae*, *Aelosomatodae*, *Aelosomatodae*, *Naidodae*, *Oposthocystidae*, *Tubibificidae*, *Phreodrolodae*, *Enchytraeidae* families.

Raw material collection of earth and/or water annelids for processing the
35 Human Skin Regenerating Ointment is done on fields or land rich in non-contaminated animal or vegetal wastes, by selecting, depending on the year season, a quantity from 150 to 800 annelids whose weight and length varies

based on the collecting season.

Once the annelids have been collected, they are washed in plastic containers with abundant deep well water and then weighed. In the winter, 200 annelids ca weigh, all together, between 150 and 400 grams, which, later, are put into
5 an aluminum, steel or iron pot exposed to low heat, the temperature of which varies between 40° a 70° degrees Celsius, for a period between 1 and 10 minutes.

50 to 70 ml or ointment is obtained in liquid, creamy or solid state, depending
10 on the state of maturity of the annelids and the working temperature.

The skin regenerator ointment is a compound of natural origin obtained through an easily executable, fast and low-cost method of extraction, providing great advantages to the pharmaceutical and cosmetic industries.
15

The annelid-extract obtained by the present invention serves to prepare useful compositions for treating dermatological affections, such as: hot water or fire burns, healing of injuries (new or old), scores; at surgical level (tissue regeneration after operations); reinforcement of muscle tissues; at cosmetic
20 level, skin strengthening, pigmentation improvement, and protection against radiation and oxidizing agents

In the prior art, the treatment applied to a first or second degree burn from fire, hot water or any element in contact with a hand, is the use of medicines
25 containing: (benzocaine (infection), analgesics (pain), anti inflammatories (inflammation), vitamin E (skin regeneration), (valine and isoleucine (tissue repair and production of (L-Glutamine), which means, at least, three different medicines applied on a single burn.

30 The advantage of the present invention is that the annelid extract used to prepare a skin regenerating ointment has various simultaneous active principles, since the skin regenerating ointment prevents infection, and acts both as an anti-inflammatory and a skin regenerator.

35 Using the skin regenerator obtained from annelids only requires the additional use of analgesics during the first day of treatment, which presents a great advantage with respect to the already described compositions for treating

burns, in addition to the easy-to-produce and low-cost advantages.

Other relevant advantages of the preset invention are: low cost, fast attainment of the raw material and easy preparation of the extract. The attainment of annelids to prepare the extract presents great advantages with respect to other inventions based on the extraction of natural products, such as emu oil. The attainment of annelids has advantages, not only the easy acquisition of these organisms from earth and water, but also because the farming of annelids is known for other purposes, and has been widely developed, living place to worm farming, annelids show a high reproduction rate, they reproduce at an average rate on 1 to 20 individuals per year and, in adequate condition, they may breed at a rate of 1,000 to 4,000 individuals per square meter of earth..

One comparative advantage is that the extract of the present invention shows a composition having a mono- and poly-saturated oil content much higher than emu oil and other natural extracts used for skin care treatment.

Another comparative advantage with respect to emu oil, is the high content of Omega 3 oil in the annelid extract as compared to the emu oil used in skin care treatments.

Another advantage is the effect the extract exerts not only at dermis level, but also at the epidermis one.

EXAMPLE 1

Production of a human skin regenerating extract.

The base raw material for this example is earth annelids of the prosopore, opistopore family, *Lumbricullina*, *Haplotaxina*, *Lumbricina* and *Megascolecina* type.

1. Earth annelids were collected on land abundant with non contaminated animal or vegetal wastes, located in the San Patricio sector, Cautín Province, Araucanía Region, Chile.
2. 200 annelids specimens were obtained, which were washed in plastic containers with abundant untreated water (non-chlorinated, from a deep well).
3. The annelids were washed and weighed, and 190 g. were obtained,

which were subject to a temperature from 45° to 65° C, in a 1 liter stainless steel container, for a 10-minute period.

4. A final quantity of 70ml was obtained. This extract may be used directly as a skin regenerating ointment or for preparing a composition containing pharmaceutically acceptable additives, known in the state of the art in compositions for dermatological purposes.

Composition of the extract obtained

Table I: Annelid extract composition

Components	Percentage
Proteins	68.71%
Lipids	6.88%
Ashes	0.72%
Raw fiber	Not found
Carbon Hydrates	18.61%

Analysis on a 200-annelid sample, conducted by Laboratorio Diamolab Ltda.

Table II: Annelid amino-acid extract composition

Aminoacid Profile	Result g/100g
ASPARTIC ACID	0.135
GLUTAMIC ACID	0.123
HYDROXYPROLINE	0.065
SERINE	0.056
GLYCINE	0.322
HISTIDINE	0.025
ARGININE	lower than 0.01
TAURINE	lower than 0.01
TREONINE	0.093
ALANINE	0.311
PROLINE	0.064
TYROSINE	0.05
VALINE	0.251
METHIONINE	0.014
ISOLEUCINE	0.211
LEUCINE	0.297

PHENYLANINE	0.162
LYSINE	0.032

The Skin Regenerating ointment contains 90% of essential human amino-acids.

Table III: Composition of the saturated fatty acids in the annelid extract

Saturated fatty acid Profile	Results % methyl esters
C11:0 Undecanoic	1.62
C12:0 Lauric	5.38
C 13:0 Tridecanoic	3.07
C14:0 Miristic	2.36
C 16:0 Palmitic	5.12
C 17:10 Heptadenoic	1.97
C 18:0 Estearic	8.1
C 22:0 Docasenoic	1.09
C 24: 0 Tetracosenoic	0.84
Total	29.55

5

Table IV: Mono-saturated fatty acid composition in annelid extract

Mono-saturated fatty acid Profile	Results % methyl esters
C12:1 Dodecanoic	7.25
C13:1 tridecanoic	1.63
C 14:1W9 Miristeloic	2.34
C14:1W7 Miristeloic	1.14
C 15: 1Pentadeccuenoic	0.98
C 16:1 W9 Palmitoleic	2.41
C 16:1 W7 Palmitoleic	3.19
C 16:1 W6 Palmitoleic	1.27
C 17: 1 W9 heplatecanoic	1.18
C18 :1 W9 Oleic	2.43
C18 :1 W7 Oleic	8.07
C 20:1 W11 Eicosaenoic	8.47
C 22: 1W11 Docasenoic	0.88
Total	41.24

Table V: Poly-saturated fatty acid composition in annelid extract

Poly-saturated fatty acid Profile	Results % methyl esters
C16: 2 Hexadecadenoic	2.82
C16:3 Hexadecatrienoic	1.8
C 18:2 W6 Linoleic	5.28
C 18:3 W6 Linoleic	2.5
C 20: 2 W6 Eicosadienoic	1.6
C 20:3 W6 Eicosatrienoic	0.87
C 20:4 W6 Eicosatrienoic	8.18
C 20:5 W3 Eicosapentaenoic	6.17
Total	29.22

- 5 Analysis conducted by ANALAB CHILE S.A, as report on results Nr. 161968, dated 01-06-2006.

The concentration of fatty and saturate acids in the annelid extract obtained is low, but it is high in mono-saturated and poly-saturated oils.

10

EXAMPLE 2

Use of annelid extract to treat skin burns.

- In a farm, in the borough of Vilcún, a worker, aged 37, together with two other workers, was painting a shed cover with hot tar, when a zinc roof tile suddenly collapsed and he and the hot tar bucket fell from a 10-meter height. The left side of his face and part of his scalp got covered with a film of hot tar, which was partly removed by his workmates, and the rest of the material was removed at the Vilcún and Temuco hospitals.

- 20 After the accident, he remained in hospital for 3 months due to 2nd and 3rd degree burns, after which period he was released until the infection and pain had been controlled. No skin change or face skin regeneration treatment was carried out.

- 25 He continued an out-patient treatment with only disinfectants and analgesics. After 2 months of out-patient treatment, the treatment applied at Temuco's

Hernán Henríquez hospital was discontinued. The patient had pain and great sensibility on the affected areas and the burns had healed.

5 Based on this condition, the ointment of the invention, annelid extract, was applied on a daily basis.

The annelid extract was obtained on a daily basis by heating two annelids in a 15 ml capacity stainless steel container.

10 Heating took place in a furnace or in a thermal-regulated bath.

The extract obtained was directly applied on the skin, being manually spread on face and head, on the damaged part, twice a day, over a three-month period.

15

The results, after a three-month long treatment were as follows:

- Face skin recovery on the affected zone.
- Recovery of part of the scalp lost as a result of the burn.
- Recovery of skin pigmentation and strength.

20

The annelid extract of the present invention did not regenerate part of the lost ear due to the effect of the hot tar, and no hair was regenerated on the rear part of the head, where the greatest damage took place and the burn was deeper (3rd degree).

25

The additional advantages of applying the annelid extract, over the three-month long treatment were that the patient did not suffer from infections on the injure and pains disappeared.

30 **EXAMPLE 3**

Use of annelid extract to treat injuries.

The annelid extract obtained was applied on field workers' minor injuries. The kind of injuries treated is from damaged caused by barbed wire on the workers' hands, back and head, which take place when these workers have to
35 release animals entangled in fences.

The extract applied is obtained by heating two annelids in a 15 ml capacity

stainless steel container inside a furnace at 40-60 °C.

- The treatment on injuries at dermis level consisted of the application, twice a day (morning and afternoon), of the extract for three days, period in which
- 5 injuries properly healed. These injuries were treated with annelid extract as the only treatment, without applying other skin regenerating compositions or analgesics.

CLAIMS

1. A pharmaceutical or cosmetic composition comprising annelid extracts.
2. The pharmaceutical or cosmetic composition in accordance with claim 1,
5 wherein the annelid extract comes from earth annelids and/or water annelids.
3. The pharmaceutical or cosmetic composition in accordance with claim 1, wherein it comprises an annelid extract that is additive-free.
4. The pharmaceutical or cosmetic composition, in accordance with claim 1,
10 wherein the annelid extract comprises about 70% of proteins, about 7% of lipids, about 20% of carbon hydrates, and about 0.7% of ashes.
5. The pharmaceutical or cosmetic composition, in accordance with claim 4, wherein the lipid fraction comprises about 30% of saturated fatty acids, about 40% of fatty mono-saturated acids, and about 30% of fatty poly-saturated acids.
- 15 6. A Method of preparing a pharmaceutical or cosmetologic composition wherein it comprises the collection of annelids and attainment of the extract from annelids which are the raw material of said composition.
7. The method of preparing a pharmaceutical or cosmetologic composition, in accordance with claim 6, wherein the collection of annelids comprises
20 earth annelids and/or water annelids.
8. The method of preparing a pharmaceutical or cosmetologic composition, in accordance with claim 6, wherein the extract is attained through the steps of:
 - washing the annelids with chlorine-free water, and
 - 25 • heating the collected annelids.
9. The method of preparing a pharmaceutical or cosmetologic composition, in accordance with claim 8, wherein heating is applied at a 45° to 65° C temperature range.
10. The method of preparing a pharmaceutical or cosmetologic composition,
30 in accordance with claim 8, wherein heating is applied for a 1 to 10-minute period.
11. Use of the pharmaceutical composition of claim 1 for the manufacture of a medicament for treating dermatological affections and for surgical or cosmetologic treatments.
- 35 12. Use in accordance with claim 11, for the manufacture of a medicament for treating dermis and epidermis affections.