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(71) Applicant *(for all designated States except US)*: **GALDERMA RESEARCH & DEVELOPMENT** [FR/FR]; 2400 route des Colles, Les Templiers, F-06410 Biot (FR).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **ANDRES, Philippe** [FR/FR]; 126, avenue des Termes, F-06530 Peymeinade (FR). **MARTEL, Philippe** [FR/FR]; Villa de Green Side n° 9, 210, avenue Saint Philippe, F-06410 Biot (FR).

(74) Agent: **ALLAB, Myriam**; L'Oreal, River Plaza - DIPI, 25-29 quai Aulagnier, F-92665 Asnières-sur-Seine (FR).

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(54) Title: DEPIGMENTING TOPICAL COMPOSITIONS AND THEIR USES

(57) Abstract: The present invention relates to the use of rucinol or one of its salts at a concentration of 3% to 10% and preferably of 3% to 5% in a topical composition, the said composition being intended to whiten human skin or to whiten non-scalp hair or scalp hair.

DEPIGMENTING TOPICAL COMPOSITIONS AND THEIR USES

The present invention relates to the use of rucinol or one of its salts at a concentration of 3% to 10% and preferably of 3% to 5% in a topical composition, the said composition being intended to whiten human skin or to whiten non-scalp hair or scalp hair.

The colour of the human skin depends on various factors and in particular on the seasons of the year, race, age and sex; it is mainly determined by the nature and the concentration of melanin produced by the melanocytes. Melanocytes are specialized cells which synthesize melanin via specific organelles, the melanosomes.

The colour of the skin, non-scalp hair and scalp hair is due to melanin; when the skin, non-scalp hair or scalp hair are dark, some people wish to see these lighter. This is particularly advantageous for non-scalp hairs which are less visible when they are light than when they are dark.

The use of harmless topical depigmenting substances which are highly effective is very particularly sought after.

The substances most widely used as depigmenting agents are more particularly hydroquinone and its derivatives, in particular its ethers, such as hydroquinone monomethyl ether and monoethyl ether. These compounds, although they exhibit a degree of effectiveness, are not, unfortunately, devoid of side effects due to their toxicity, which can make it problematic, indeed even dangerous, to employ them. This is because this toxicity can be permanent, with disappearance of the melanocytes from the region and consequently permanent hypo- or depigmentation (confetti-like dermatitis).

Thus, hydroquinone is a compound which is particularly irritating and cytotoxic for the melanocyte, the total or partial replacement of which

has been envisaged by many authors.

Use is commonly made, as inhibitor of the activation of tyrosinase, of kojic acid, which complexes the copper present in the active site of this enzyme. Unfortunately, this compound is unstable in solution, which significantly complicates the manufacture of the composition.

There may be various motivations which drive the decolouring of the skin. Plain lightening of the complexion is often desired in Black Africa and in Asian countries, with conventional or chemical solutions which generally exhibit significant harmful side effects on the appearance and the structure of the skin.

The paleness or the whiteness of the Asian face is obtained with molecules, such as arbutin, kojic acid or ascorbic acid, which may be poorly tolerated or irritating.

There thus exists a need to be able to decolour a normally pigmented skin in order to increase the radiance of the complexion or in order to render uniform the appearance of the skin.

Rucinol is used in cream and serum compositions at a concentration of 0.3% (Iklen® Cream and Serum, sold by Merck Médication Familiale) as depigmenting product for the treatment of certain disorders of pigmentation, such as lentigines and melasma. These products are not in any way used to modify the constitutional pigmentation of the skin, a natural phenomenon which is completely different from a hyperpigmentation phenomenon.

There thus exists a need to have available compositions exhibiting a good whitening activity which are well tolerated by the skin, in particular for non-Caucasian skin, such as Hispanic, Indian, black, Asian or mixed race skin.

In this respect, the Applicant Company has discovered, surprisingly and unexpectedly, that rucinol at a concentration of between 3 and 10% by weight, with

respect to the total weight of the composition, and preferably between 3 and 5% by weight, with respect to the total weight of the composition, makes it possible to obtain a significant decrease in constitutional pigmentation and thus to obtain a good whitening activity, without detrimentally affecting the safety profile of the composition in comparison with the 0.3% rucinol concentration.

A subject-matter of the present invention is thus a topical composition intended for the whitening of the skin, characterized in that it comprises, in a physiologically acceptable medium, rucinol or one of its salts present at a concentration ranging from 3 to 10% by weight and preferably from 3 to 5% by weight, with respect to the total weight of the composition.

Another subject-matter of the present invention is the use of rucinol or one of its salts at a concentration ranging from 3 to 10% by weight and preferably between 3 and 5% by weight and more preferably of 5% by weight, with respect to the total weight of the composition, in a topical composition as agent for whitening the skin and/or non-scalp hair and/or scalp hair. The topical composition will preferably be used as whitening agent for the skin.

Rucinol is also known as lucinol or 4-(n-butyl)-resorcinol.

Rucinol salts is understood to mean in particular salts formed with a pharmaceutically acceptable base, in particular an inorganic base, such as sodium hydroxide, potassium hydroxide and ammonia, or an organic base, such as lysine, arginine or N-methylglucamine, but also the salts formed with fatty amines, such as dioctylamine, aminomethyl propanol and stearylamine.

Preferably, rucinol will be used.

Constitutional pigmentation is understood to mean the natural pigmentation of the skin.

Significant decrease is understood to mean a decrease in the colour of the skin which is clearly

identifiable to the naked eye in comparison with an adjacent skin area not treated with the active principle.

The present invention also relates to the use of a topical composition intended to limit browning of the skin, characterized in that it comprises, in a physiologically acceptable medium, rucinol or one of its salts present at a concentration ranging from 3 to 10% by weight, preferably from 3 to 5% by weight, with respect to the total weight of the composition.

Browning of the skin is understood to mean the change in complexion of the skin towards a darker colour.

Another subject-matter of the invention is a cosmetic method for whitening human skin and/or for whitening non-scalp hair and/or scalp hair which comprises the application, to the skin and/or non-scalp hair and/or scalp hair, of a cosmetic composition comprising rucinol or one of its salts present at a concentration ranging from 3 to 10% by weight and preferably from 3 to 5% by weight, with respect to the total weight of the composition.

Topical composition is understood to mean a composition intended to be applied to the skin and/or mucous membranes.

Physiologically acceptable medium is understood to mean a medium compatible with the skin, mucous membranes and/or superficial body growths.

A clinical study was carried out by the Applicant Company on the skin tolerance of three compositions comprising different concentrations of rucinol. A preceding study showed that concentrations ranging up to 5% are well tolerated (results not shown). The composition comprising rucinol at 0.3% (Iklen® cream) 2% or 5% by weight, with respect to the total weight of the composition, was applied once daily for 26 days to an area of 20 cm^2 on the cheek of a healthy subject. The treated areas of 36 healthy subjects were clinically evaluated every day.

The tolerance was determined by physical evaluation (erythema, skin dryness, desquamation and oedema) and functional signs (smarting, burning, itching).

The results of the study have shown that the compositions according to the invention whiten the skin in a uniform manner in some treated subjects over the entire surface area of application of the composition, mainly with the rucinol concentration of 5%.

This whitening is not observed in a significant manner with the cream comprising 0.3% of rucinol.

The study also showed that the compositions according to the invention are well tolerated and do not exhibit more side effects than with the 0.3% rucinol composition.

The composition can then comprise all the constituents normally employed in the application envisaged.

Of course, a person skilled in the art will take care to choose this or these optional additional compounds and/or their amounts so that the advantageous properties of the compounds according to the invention are not, or not substantially, detrimentally affected by the envisaged addition.

The composition according to the invention can be provided in all the formulation forms normally used in the cosmetic and dermatological fields; it can be more or less fluid and have the appearance of a white or coloured cream, of a salve, of a milk, of a lotion, of a serum, of a paste or of a foam. It can optionally be applied to the skin or to the scalp hair in the form of an aerosol. It can also be provided in the solid form, for example in the form of a stick. It can be used as care product and/or as make-up product. It can also be in a shampoo or conditioner form.

This composition can form a cleaning, protecting, treating or care cream for the face, for the hands, for the feet, for the major anatomical folds or for the body (for example, day creams, night creams, make-up-

removing creams, cream foundations or sun creams), a liquid foundation, a make-up-removing milk, a protective or care body milk, a sun milk or a lotion, gel or foam for caring for the skin, such as a cleansing lotion.

The following examples illustrate the invention without limiting the scope thereof. The compounds are, as the case may be, mentioned under chemical names or under CTFA (International Cosmetic Ingredient Dictionary and Handbook) names.

Example 1

A whitening cream for the care of the face of oil-in-water emulsion type is prepared, which cream comprises (% by weight):

Rucinol	3%
Glycerol stearate	2%
Polysorbate 60 (Tween 60 from ICI)	1%
Stearic acid	1.4%
Triethanolamine	0.7%
Carbomer	0.4%
Hydrogenated polyisobutene	12%
Perhydrosqualene	12%
Glycerol	5%
Antioxidant	0.05%
Preservative	q.s.
Water	q.s. for 100%

Example 2

A whitening gel for the skin is prepared, which gel comprises (% by weight):

Rucinol	5%
Hydroxypropylcellulose (Klucel H from Hercules)	1%
Antioxidant	0.05%
Isopropanol	40%
Preservative	q.s.
Water	q.s. for 100%

CLAIMS

1. Topical composition intended for whitening human skin and/or its superficial body growths, characterized in that it comprises, in a physiologically acceptable medium, from 3 to 10% by weight of rucinol or one of its salts, with respect to the total weight of the composition.

2. Composition according to Claim 1, characterized in that rucinol or one of its salts is present in an amount ranging from 3 to 5% by weight, with respect to the total weight of the composition.

3. Use of rucinol or one of its salts at a concentration of 3 to 10% by weight, with respect to the total weight of the composition, in the preparation of a topical composition for whitening the skin and/or its superficial body growths.

4. Use according to Claim 3, characterized in that the composition is used to whiten human skin.

5. Use according to Claim 3 or 4, characterized in that rucinol or one of its salts is present at a concentration ranging from 3 to 5% by weight, with respect to the total weight of the composition.

6. Use of a topical composition intended to limit browning of the skin, characterized in that it comprises, in a physiologically acceptable medium, rucinol or one of its salts present at a concentration ranging from 3 to 10% by weight, with respect to the total weight of the composition.

7. Cosmetic method for whitening human skin and/or its superficial body growths, characterized in that it consists in applying, to the skin and/or superficial body growths, a composition described according to Claim 1 or Claim 2.

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2009/064239

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K8/34 A61Q19/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61K A61Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

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"A" document defining the general state of the art which is not considered to be of particular relevance

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
27 January 2010	04/02/2010

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Simon, Frédéric

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International application No
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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

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INTERNATIONAL SEARCH REPORT

Information on patent family members

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