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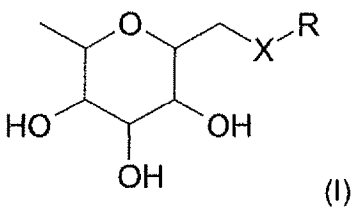
(54) **Title:** USE OF A D- AND L-FUCOSE-DERIVED C-GLYCOSIDE COMPOUND AS AN AGENT FOR ACTIVATING AND REGULATING CUTANEOUS IMMUNITY



(I)

(57) **Abstract:** The present invention relates to the use of compounds of general formula (I) derived from D- and L-fucose: as agents for stimulating the immune system of the skin and/or as immunoregulators, and for preparing a composition containing a cosmetically or pharmaceutically acceptable medium, intended in particular to prevent and/or limit the appearance of cutaneous immune imbalances, in particular related to environmental stresses.

Use of a D- and L-fucose-derived C-glycoside compound as an agent for activating and regulating cutaneous immunity

The present invention relates to the use of D- and L-fucose-derived C-glycoside compounds as agents for stimulating the immune system of the skin and/or as immunoregulators, and for preparing a composition containing a cosmetically or pharmaceutically acceptable medium, intended in particular to prevent and/or limit the appearance of cutaneous immune imbalances, in particular related to environmental stresses.

Cutaneous immune disorders are normal physiological phenomena which appear with age. They can, however, be accelerated by infections with microorganisms (viruses and bacteria), stress, chronological ageing, ultraviolet rays, "urban" living conditions, etc.

The immune system comprises a collection of specialized cells which are subject to multiple control mechanisms that ensure their renewal, their activation and their differentiation, and are essential to a normal level of immunocompetence. The role of the immune system is to discriminate self from non-self in order to eliminate pathogenic agents and spontaneous tumours. Any cellular depletion, any incorrect immune regulation or any functional deficiency is liable to promote the occurrence of manifestations which range from discomfort to pathological disorders characterized by the disturbance of the mechanisms of recognition of self with respect to non-self, and a greater sensitivity with respect to microbial attacks and neoplastic processes.

The skin is an organ that is highly important for the organism and is recognized as one of the main active elements of the immune defence system. Three epidermal

cell types participate in this system: keratinocytes, melanocytes and Langerhans cells. These cells, which are found only in the skin, play an essential role in the immune response, and in particular in antigen presentation.

Normal skin constitutes a barrier and is capable of defending itself against outside attacks, in particular chemical and mechanical attacks; in this respect, a certain number of defence reactions against environmental factors (climate, ultraviolet rays, tobacco, pollutants, etc.) and/or xenobiotics (such as, for example, certain medicaments) occur therein.

Various factors, such as atmospheric pollutants, detergents, allergens, UV radiation, etc., negatively affect, by virtue of their action on the skin, a variety of immune responses, both locally at the site of exposure, and systemically, at distant sites. This form of immunosuppression is in particular related to the induction of antigen-specific suppressor T cells. Impairment of the delayed response is particularly important since immune reactions generated by T lymphocytes are responsible for protection against many chronic infectious pathologies.

Pathologies also exist which are based not on an insufficiency of immune cells, but on an immune imbalance; this is the case, in particular, of atopic diseases and autoimmune diseases which present, respectively, an excess of Th-2 lymphocytes and an excess of Th-1 lymphocytes.

The prevalence of atopic diseases (accompanied by an excessive presence of Th-2-type lymphocytes, such as atopic dermatitis, gastrointestinal allergies, allergic rhinitis and conjunctivitis, asthma) and of autoimmune diseases (accompanied by an excessive presence of Th-1-type lymphocytes, such as psoriasis, vitiligo, diffuse

scleroderma, lupus erythematosus, certain forms of alopecia, rheumatoid arthritis, type I diabetes) has gradually increased over the last few decades in western societies.

The explanation which has appeared to be the most plausible regarding the increase in Th-2-related conditions is the hygiene-related hypothesis which suggests that the rapid increase in atopic eczemas is related to the current cleanliness of environments and to the decrease in exposure to microorganisms at the beginning of life (Holt PG, in Nestlé Nutrition Workshop series Pediatric Program, Isolauri E et al ed, Allergic diseases and the environment, Karger AG, Basel, vol 53 pp 53-68, 2004).

During the allergic reaction, which can be explained by a reorientation of Th-1-type immune reactions towards Th-2-type responses, the interaction between the normal host and the allergen is altered. The allergic reaction is then accompanied by an imbalance in the immune response, which may then be induced by resident bacteria (Martinez FD, Respir Res: 2:129-132, 2001).

These atopic conditions are chronic and often systemic inflammatory reactions of complex origin (genetic and environmental factors). In these pathologies, the responses of type 2 (Th-2) T helper cells to "inoffensive" antigens (allergens) of the environment play a determining role in triggering allergic conditions (Romagnani S, Curr Opin Immunol 6:838-846, 1994). Th-2 cells explain the joint intervention, in the allergic inflammatory process, of B cells that produce E immunoglobulins (via the production of interleukins IL-4 and IL-13), and of mast cells (via the production of IL-5).

Moreover, it is also important to emphasize that, while there is currently an increase in allergic pathologies

related to Th-2-type cells, at the same time, an increase in pathologies related to Th-1 cells (autoimmune diseases, such as type I diabetes, psoriasis or vitiligo) is observed in developing countries.

Th-1-type cells play an important role in the development of the delayed hypersensitivity reaction (DHR); thus, in certain chronic autoimmune diseases such as rheumatoid arthritis and thyroiditis, the skin lesions observed are of the DHR type, and the CD4 T cells within said lesions are mainly of the Th-1 type. Identical results have been obtained over the course of infectious diseases due to mycobacteria (tuberculosis, leprosy), over the course of Lyme disease and over the course of psoriasis.

Vitiligo is an acquired depigmentation disorder of the skin that affects 1% of the world's population, regardless of skin colour. Vitiligo is a skin disease in which the melanocytes (MCs) are eliminated from the basal layer of the epidermis in the lesions. This disappearance of melanocytes leads to a deficient pigmentation. In vitiligo lesions, the melanocytes are destroyed by MC-reactive T cells. The depigmentation frequently begins during adolescence.

For example, after an infection, UV radiation or a chemical/mechanical attack, the melanocytes are damaged. Under conditions of normal immune control, these impairments are controlled by the immune system which destroys the modified cells. In the case of vitiligo, these impairments are not correctly treated and they constitute a source of autoantibodies which will contribute to establishing the autoimmune pathology.

Thus, it appears that a therapy which would make it possible to reorient the Th-2 "allergic" or Th-1

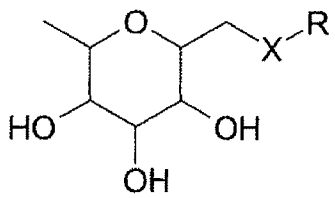
"autoimmune" immune response towards a physiological balance would lead to products whose topical application could induce a regulation of local immune phenomena.

The applicant has now demonstrated that C-glycoside compounds of general formula (I) are capable both of stimulating the immune system of the skin and also of rectifying an immune imbalance between populations of Th-1 and Th-2 lymphocytes, and are capable of causing atopic or autoimmune disorders.

It is known that certain sugars such as aldoses, ketoses, deoxyoses or monosaccharide derivatives stimulate immune defences (EP 0 818 201).

O-glycoside or C-glycoside molecules which modulate the immune system also exist, such as C-glycolipid compounds (WO 2003/105769), fucopeptides and amido-deoxygalactose derivatives (US 5,962,660 and WO 96/29339).

The present invention relates to the use of compounds of general formula (I):



(I)

in which,

- X represents a group chosen from: -CO-, $-CH(NR_1R_2)-$, -CHR'- and -C(=CHR')-;
- R represents a linear or branched, saturated or unsaturated alkyl, perfluoroalkyl or hydrofluoroalkyl chain, or a cycloalkyl, cycloperfluoroalkyl or cyclohydrofluoroalkyl ring, containing from 1 to 18 carbon atoms, or a phenyl radical, it being

possible for said chain, said ring or said radical to be optionally interrupted with one or more heteroatoms chosen from oxygen, sulphur, nitrogen and silicon, and optionally substituted with at least one radical chosen from $-OR'_1-$, $-SR''_1$, $-NR'''_1R'_2$, $-COOR''_2$, $-CONHR'''_2$, -CN, halogen, perfluoroalkyl and hydrofluoroalkyl, and/or at least one cycloalkyl, aryl or heterocyclic radical, optionally substituted;

- R', R_1 and R_2, which may be identical or different, have the same definition as that given for R, and can also represent a hydrogen and a hydroxyl radical;
- R'_2 and R'''_2, which may be identical or different, represent a hydrogen atom, or a radical chosen from a hydroxyl radical and a linear or branched, saturated or unsaturated alkyl, perfluoroalkyl and/or hydrofluoroalkyl radical containing from 1 to 20 carbon atoms;
- R'_1, R''_1, R''_2 and R'''_1, which may be identical or different, represent a hydrogen atom, or a radical chosen from a linear or branched, saturated or unsaturated alkyl, perfluoroalkyl and/or hydrofluoroalkyl radical containing from 1 to 20 carbon atoms;

with the following restrictions:

- R1 and R2 cannot simultaneously be a hydroxyl;
- R''_1 and R'_2 cannot simultaneously be a hydroxyl;
- when S is L-fucose and X is =CO, then R cannot be a $-CH_3$ or an unsubstituted phenyl;

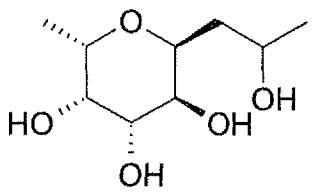
for combating the weakening of the natural defences of the skin which appears during chronological or photoinduced ageing and/or reinforcing the natural defences of the skin.

The C-glycoside compounds that can be used according to the invention represent a subfamily of the C-glycoside derivatives described in EP 1 345 919; they

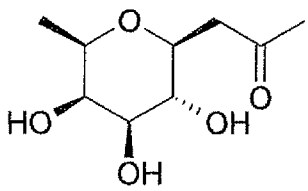
can be prepared according to the process described in said document.

Among the C-glycoside derivatives of formula (I) used according to the invention, the following are most particularly preferred:

Compound 1. 1-(C-β-L-fucopyranosyl)-2-hydroxypropane;



Compound 2. 1-(C-β-D-fucopyranosyl)propan-2-one;



Compound 3. 1-phenyl-2-(C-α-L-fucopyranosyl)-1-hydroxy-ethane;

Compound 4. 1-phenyl-2-(C-β-L-fucofuranosyl-1-hydroxy-ethane;

Compound 5. 1-phenyl-2-(C-β-D-fucopyranosyl)ethan-1-one;

Compound 6. 1-phenyl-2-(C-β-D-fucopyranosyl)-1-hydroxy-ethane;

Compound 7. 1-phenyl-2-(C-α-D-fucopyranosyl)ethan-1-one;

Compound 8. 1-phenyl-2-(C-α-D-fucopyranosyl)-1-hydroxy-ethane.

More particularly, the use of the C-glycosides of general formulae (I) according to the invention is suitable for preparing the skin against exposure to the sun.

Thus, the use according to the invention makes it possible to prevent and/or limit the harmful effects of exposure to UV rays.

The C-glycosides of general formulae (I) can also be used for maintaining a balance between Th-1 and Th-2 lymphocyte populations and/or for correcting an immune imbalance related to an excess of Th-1-type lymphocytes or Th-2-type lymphocytes.

These compounds according to the invention may therefore be advantageously used for combating undesirable manifestations of atopic type, in particular for treating reactive skin (characterized by red blotches, painful sensations, swelling), for preventing and/or decreasing itching, or else combating autoimmune conditions such as an imbalance in pigmentation of the skin and/or of the hair, in particular hair turning white or grey prematurely.

According to another of its subjects, the present invention relates to the use of C-glycoside compounds of general formulae (I), for preparing a composition, comprising a physiologically acceptable medium, for use in the prevention and/or treatment of cutaneous autoimmune diseases or cutaneous atopic disorders.

More particularly, the cutaneous atopic disorders are chosen from cutaneous allergic reactions, atopic dermatitis and atopic eczema, and the cutaneous autoimmune diseases are chosen from delayed contact hypersensitivity, psoriasis, vitiligo, diffuse scleroderma, lupus erythematosus or certain forms of alopecia.

The term "immunostimulant agent" is intended to mean a compound whose administration to an organism results in the proliferation of the immune cells of said organism, for example the lymphocytes.

The term "immunoregulatory agent" is intended to mean an agent capable of maintaining and/or reestablishing a cutaneous immune balance between Th-1-type and Th-2-type cell populations, or else of correcting an excessive presence of Th-1-type or Th-2-type cells.

An immune imbalance may in particular be demonstrated by virtue of the increase, in an organism, of one or more cytokines characteristic of a lymphocyte type.

In fact, in addition to their classification according to the structure of their T receptor, Th-1-type and Th-2-type lymphocytes have been classified according to their cytokine protocol.

The cytokines characteristic of type 1 (Th-1) lymphocytes are IL-2, IFN-γ and TNF-β. The cytokines of type 2 (Th-2) lymphocytes are IL-4, IL-5, IL-9, IL-10 and IL-13.

More generally, the C-glycoside compounds of general formulae (I) can be used as an immunostimulant medicament in humans or in animals.

For this type of use, the compositions comprising the C-glycoside compounds of general formulae (I) can be administered, for example, parenterally, (intraperitoneally, subcutaneously, intramuscularly, intravenously, percutaneously), orally, nasally, conjuctivally, rectally or perlingually.

They can also be used by local application, for example by means of orally disintegrating tablets, in particular in non-specific immunotherapy of oral cavity diseases.

The medicament of the invention can be administered by way of prophylaxis, in the various cases above, and in

particular for the prevention of recurring infections of the ear, nose and throat (ENT) sphere, and for the prevention of risks of infection in chronically ill patients.

The medicament of the invention is administered in particular as an immunostimulant treatment, in the ENT or bronchopulmonary field (rhinopharyngitis, laryngitis, sinusitis, sore throats, otitis, bronchitis, etc.) or in the dermatological field, in the case of bacterial, fungal or viral infections.

Preferably, the C-glycoside compound of general formulae (I) according to the invention will be formulated in a cosmetic or pharmaceutical composition intended to be applied topically to the skin, the scalp or the mucous membranes.

The compositions used according to the invention can be in any of the forms suitable for the applications envisaged, in particular topical application, in the cosmetics and dermatological fields.

The composition according to the invention contains a physiologically acceptable medium and one or more compounds according to the invention in an effective amount for stimulating the immunity of the skin or for reequilibrating the balance between Th-1 and Th-2 lymphocytes, for example in an amount ranging from 0.01% to 30% by weight, and preferably from 0.1% to 5% by weight, relative to the total weight of the composition.

The term "physiologically acceptable medium" is understood to mean a medium compatible with the skin and, optionally, with the mucous membranes, the nails, the scalp and/or the hair.

The composition according to the invention can be in the form in particular of an aqueous solution or a dispersion of the lotion or serum type, emulsions with a liquid or semi-liquid consistency, of the milk type, obtained by dispersion of a fatty phase in an aqueous phase (O/W) or vice versa (W/O), or suspensions or emulsions which are soft in consistency, of the aqueous or anhydrous gel or cream type, or else microcapsules or microparticles, or vesicular dispersions of ionic and/or non-ionic type. These compositions are prepared according to the usual methods.

This composition may be more or less fluid and may have the appearance of a white or coloured cream, an ointment, a milk, a lotion, a serum, a paste or a foam. It can optionally be applied to the skin in the form of an aerosol. It can also be in the form of a solid, for example in the form of a stick. It can be used as a care product, as a cleansing product, as a makeup product or alternatively as a shampoo or conditioner.

When the composition that can be used according to the invention is an emulsion, the proportion of the fatty phase can range from 5% to 80% by weight, and preferably from 5% to 50% by weight, relative to the total weight of the composition. The oils, the waxes, the emulsifiers and the coemulsifiers used in the composition in the form of an emulsion are chosen from those conventionally used in the cosmetics field. The emulsifier and the coemulsifier are present, in the composition, in a proportion ranging from 0.3% to 30% by weight, and preferably from 0.05% to 20% by weight, relative to the total weight of the composition. The emulsion can also contain lipid vesicles.

The composition according to the invention can be intended for a cosmetic or pharmaceutical, particularly dermatological, application. The composition according

to the invention is preferably intended for a cosmetic application.

A subject of the invention is therefore also a cosmetic treatment process for the skin or for the scalp, comprising the topical application to the skin or the scalp of the composition described above.

Given the immunostimulant and equilibrating properties of the compounds according to the invention, this process is, in particular, intended to reinforce the natural defences of the skin and to improve the cutaneous immune balance.

The C-glycoside compounds according to the invention will advantageously be combined with active agents for the hair, chosen from:

- anti-seborrhoeic agents, such as certain sulphur-containing amino acids, 13-cis-retinoic acid or cyproterone acetate;
- agents for combating squamous states of the scalp (dandruff), such as zinc pyrithione, selenium disulphide, climbazole, undecylenic acid, ketoconazole, piroctone olamine (octopirox) or cyclopiroctone (cyclopirox);
- active agents for stimulating hair regrowth and/or promoting the slowing down of hair loss; mention may more particularly be made, in a non-limiting manner, of:

  * nicotinic acid esters, including in particular tocopheryl nicotinate, benzyl nicotinate and C_1-C_6 alkyl nicotinates, for instance methyl nicotinate or hexyl nicotinate;
  * pyrimidine derivatives, such as 2,4-diamino-6-piperidinopyrimidine 3-oxide or "Minoxidil" described in patents US 4,139,619 and US 4,596,812; Aminexil or 2,4-diaminopyrimidine 3-oxide described in WO 96/09048;
  * agents that are both lipoxygenase inhibitors and cyclooxygenase inducers, or cyclooxygenase-inducing

agents that promote hair regrowth, such as those described by the applicant in European patent application EP 0 648 488;

- antibiotics such as macrolides, pyranosides and tetracyclines, and in particular erythromycin;
- cinnarizine, nimodipine and nifedipine;
- hormones, such as estriol or the like, or thyroxine and salts thereof;
- antiandrogenic agents, such as oxendolone, spironolactone, diethylstilbestrol and flutamide;
- cromakalim and nicrorandil.

Example 1 - Demonstration of the immunostimulant activity of the C-glycoside derivatives of general formula (I)

The immunostimulant activity is tested in the following way: human peripheral blood cells are cultured in the presence of an RPMI-type culture medium supplemented with L-glutamine (2 mM), penicillin/streptomycin (50 µg/50 IU/ml) and foetal calf serum (10%). The C-glycoside derivatives are added at various concentrations (10 to 0.05 mM), as is phyto-haemagglutinin (PHA at 5 *G/ml), a positive control for lymphocyte proliferation. After 3 days of culture, the proliferation is revealed by BrdU labelling.

The results obtained are as follows:

Active agent	% stimulation relative to the control		
Concentrations (mM) →	10	5	1
Compound 1: 1-(C-β-L-Fucopyranosyl-2-hydroxypropane	129	91	136
Compound 2: 1-(C-β-D-Fucospyranosyl)propan-2-one	121	120	104

The derivatives tested exhibit a strong capacity for human lymphocyte proliferation.

Compounds 1 and 2 have a tendency to stimulate human lymphocyte proliferation at the concentration tested (between 1 and 10 mM), these compounds therefore have an immunostimulant activity.

Example 2 - Formulations

Face care gel

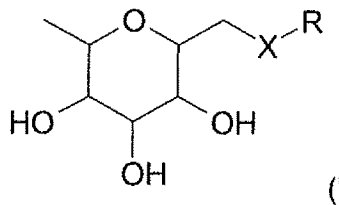
Compound 2		0.05%
Thickening polymer		1.00%
Antioxidant		0.05%
Isopropanol		40.00%
Preserving agent		0.30%
Water	qs	100%

Face lotion for hyperreactive skin

Compound 7		0.50
Magnesium gluconate		3.00
Antioxidant		0.05
Isopropanol		40.0
Preserving agent		0.30
Water	qs	100%

CLAIMS

1. Cosmetic use of at least one compound of general formula (I):



(I)

in which:

- X represents a group chosen from: -CO-, $-CH(NR_1R_2)-$, -CHR'- and -C(=CHR')-;
- R represents a linear or branched, saturated or unsaturated alkyl, perfluoroalkyl or hydrofluoroalkyl chain, or a cycloalkyl, cycloperfluoroalkyl or cyclohydrofluoroalkyl ring, containing from 1 to 18 carbon atoms, or a phenyl radical, it being possible for said chain, said ring or said radical to be optionally interrupted with one or more heteroatoms chosen from oxygen, sulphur, nitrogen and silicon, and optionally substituted with at least one radical chosen from $-OR'_1-$, $-SR''_1$, $-NR'''_1R'_2$, $-COOR''_2$, $-CONHR'''_2$, -CN, halogen, perfluoroalkyl and hydrofluoroalkyl, and/or at least one cycloalkyl, aryl or heterocyclic radical, optionally substituted;
- R', R_1 and R_2, which may be identical or different, have the same definition as that given for R, and can also represent a hydrogen and a hydroxyl radical;
- R'_2 and R'''_2, which may be identical or different, represent a hydrogen atom, or a radical chosen from a hydroxyl radical and a linear or branched, saturated or unsaturated alkyl, perfluoroalkyl and/or hydrofluoroalkyl radical containing from 1 to 20 carbon atoms;

- R'_1, R''_1, R''_2 and R'''_1, which may be identical or different, represent a hydrogen atom, or a radical chosen from a linear or branched, saturated or unsaturated alkyl, perfluoroalkyl and/or hydrofluoroalkyl radical containing from 1 to 20 carbon atoms;

with the exclusion of compounds such that:

- R1 and R2 cannot simultaneously be a hydroxyl;
- R''_1 and R'_2 cannot simultaneously be a hydroxyl;
- when S is L-fucose and X is =CO, then R cannot be a $-CH_3$ or an unsubstituted phenyl;

for combating the weakening of the natural defences of the skin which appears during chronological or photoinduced ageing and/or reinforcing the natural defences of the skin.

2. Use according to Claim 1, for preparing the skin against exposure to the sun and/or preventing and/or limiting the harmful effects of UV rays.

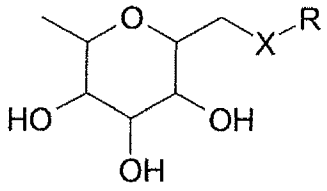
3. Use according to Claim 1, for treating reactive skin and/or preventing and/or decreasing itching.

4. Use according to Claim 1, for preventing and/or treating autoimmune disorders associated with an imbalance in pigmentation of the skin and/or of the hair.

5. Use according to Claim 4, for preventing and/or treating hair turning white or grey prematurely.

6. Use according to Claim 4 or 5, characterized in that said compound of general formula (I) is combined with at least one active agent for the hair.

7. Use of at least one compound of general formula (I):



(I)

in which:

- X represents a group chosen from: -CO-, $-CH(NR_1R_2)-$, -CHR'- and -C(=CHR')-;
- R represents a linear or branched, saturated or unsaturated alkyl, perfluoroalkyl or hydrofluoroalkyl chain, or a cycloalkyl, cycloperfluoroalkyl or cyclohydrofluoroalkyl ring, containing from 1 to 18 carbon atoms, or a phenyl radical, it being possible for said chain, said ring or said radical to be optionally interrupted with one or more heteroatoms chosen from oxygen, sulphur, nitrogen and silicon, and optionally substituted with at least one radical chosen from $-OR'_1-$, $-SR''_1$, $-NR'''_1R'_2$, $-COOR''_2$, $-CONHR'''_2$, -CN, halogen, perfluoroalkyl and hydrofluoroalkyl, and/or at least one cycloalkyl, aryl or heterocyclic radical, optionally substituted;
- R', R_1 and R_2, which may be identical or different, have the same definition as that given for R, and can also represent a hydrogen and a hydroxyl radical;
- R'_2 and R'''_2, which may be identical or different, represent a hydrogen atom, or a radical chosen from a hydroxyl radical and a linear or branched, saturated or unsaturated alkyl, perfluoroalkyl and/or hydrofluoroalkyl radical containing from 1 to 20 carbon atoms;
- R'_1, R''_1, R''_2 and R'''_1, which may be identical or different, represent a hydrogen atom, or a radical chosen from a linear or branched, saturated or unsaturated alkyl, perfluoroalkyl and/or hydrofluoroalkyl radical containing from 1 to 20 carbon atoms;

with the exclusion of compounds such that:

- R1 and R2 cannot simultaneously be a hydroxyl;
- R''_1 and R'_2 cannot simultaneously be a hydroxyl;
- when S is L-fucose and X is =CO, then R cannot be a $-CH_3$ or an unsubstituted phenyl;

for preparing a composition, comprising a physiologically acceptable medium, for use in the prevention and/or treatment of cutaneous autoimmune diseases or cutaneous atopic disorders.

8. Use according to Claim 7, characterized in that the cutaneous atopic disorders are chosen from cutaneous allergic reactions, atopic dermatitis and atopic eczema.

9. Use according to Claim 8, characterized in that the cutaneous autoimmune diseases are chosen from delayed contact hypersensitivity, psoriasis, vitiligo, diffuse scleroderma, lupus erythematosus or certain forms of alopecia.

10. Use according to any one of the preceding claims, characterized in that said composition is intended to be applied topically to the skin, the mucous membranes or the scalp.

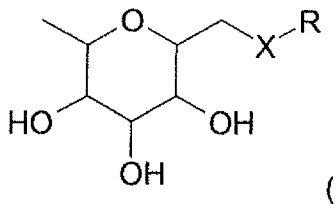
11. Use according to any one of the preceding claims, characterized in that the compound of general formula (I) is chosen from:

Compound 1. 1-(C-β-L-fucopyranosyl)-2-hydroxypropane;
Compound 2. 1-(C-β-D-fucopyranosyl)propan-2-one;
Compound 3. 1-phenyl-2-(C-α-L-fucopyranosyl)-1-hydroxy-ethane;
Compound 4. 1-phenyl-2-(C-β-L-fucofuranosyl-1-hydroxy-ethane;
Compound 5. 1-phenyl-2-(C-β-D-fucopyranosyl)ethan-1-one;
Compound 6. 1-phenyl-2-(C-β-D-fucopyranosyl)-1-hydroxy-ethane;

Compound 7. 1-phenyl-2-(C-α-D-fucopyranosyl)ethan-1-one;

Compound 8. 1-phenyl-2-(C-α-D-fucopyranosyl)-1-hydroxy-ethane.

12. Composition comprising at least one compound of general formula (I):



(I)

in which:

- X represents a group chosen from: -CO-, $-CH(NR_1R_2)-$, -CHR'- and -C(=CHR')-;
- R represents a linear or branched, saturated or unsaturated alkyl, perfluoroalkyl or hydrofluoroalkyl chain, or a cycloalkyl, cycloperfluoroalkyl or cyclohydrofluoroalkyl ring, containing from 1 to 18 carbon atoms, or a phenyl radical, it being possible for said chain, said ring or said radical to be optionally interrupted with one or more heteroatoms chosen from oxygen, sulphur, nitrogen and silicon, and optionally substituted with at least one radical chosen from $-OR'_1-$, $-SR''_1$, $-NR'''_1R'_2$, $-COOR''_2$, $-CONHR'''_2$, -CN, halogen, perfluoroalkyl and hydrofluoroalkyl, and/or at least one cycloalkyl, aryl or heterocyclic radical, optionally substituted;
- R', R_1 and R_2, which may be identical or different, have the same definition as that given for R, and can also represent a hydrogen and a hydroxyl radical;
- R'_2 and R'''_2, which may be identical or different, represent a hydrogen atom, or a radical chosen from a hydroxyl radical and a linear or branched, saturated or unsaturated alkyl, perfluoroalkyl

and/or hydrofluoroalkyl radical containing from 1 to 20 carbon atoms;

- R'_1, R''_1, R''_2 and R'''_1, which may be identical or different, represent a hydrogen atom, or a radical chosen from a linear or branched, saturated or unsaturated alkyl, perfluoroalkyl and/or hydrofluoroalkyl radical containing from 1 to 20 carbon atoms;

with the exclusion of compounds such that:

- R1 and R2 cannot simultaneously be a hydroxyl;
- R''_1 and R'_2 cannot simultaneously be a hydroxyl;
- when S is L-fucose and X is =CO, then R cannot be a $-CH_3$ or an unsubstituted phenyl;

and at least one active agent for the hair.

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2007/053356

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K31/7004 A61K8/60 A61P17/00

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 A61P

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, EMBASE, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 02/051828 A2 (OREAL [FR]; DALKO MARIA [FR]; BRETON LIONEL [FR]) 4 July 2002 (2002-07-04) page 29, line 10 - page 30, line 30 page 17, line 11 - page 20, line 12	1-6, 10-12
X	WO 02/051803 A2 (OREAL [FR]; PHILIPPE MICHEL [FR]; SEMERIA DIDIER [FR]) 4 July 2002 (2002-07-04) page 16, line 17 - page 17, line 26; examples 7,8	12
A	FR 2 861 729 A1 (FABRE PIERRE DERMO COSMETIQUE [FR]; CENTRE NAT RECH SCIENT [FR]) 6 May 2005 (2005-05-06) page 2, line 26 - page 3, line 6 page 6, line 25 page 7, lines 18-20,26,27	1-12

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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

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

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"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

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
3 July 2007	17/07/2007

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, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	TRIFILIEFF-RIOLO, S

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2007/053356

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 1 589 010 A (OREAL [FR]) 26 October 2005 (2005-10-26) page 10; example 5 page 11; example 4; table 3	1-12

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2007/053356

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		FR 2869317 A1	28-10-2005