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(54) Title: COSMETIC COMPOSITION COMPRISING NIACINAMIDE AND GINGEROL FOR THE TREATMENT OF HAIR LOSS

(57) Abstract: The present invention relates to a cosmetic composition comprising: • - at least one compound having formula (I), • - at least one gingerol, and • - optionally at least one shogaol; wherein the mass ratio of [compound having formula (l)/g ingerol] is less than or equal to 150, and when said composition comprises at least one shogaol, then the mass ratio of [gingerol(s)/shogaol(s)J is greater than or equal to 1. The invention also relates to a cosmetic treatment method comprising at least one step of applying this composition on keratin materials. The invention also relates to the non-therapeutic cosmetic use of this combination of active agents to induce and/or stimulate the growth of keratin fibers and/or impede their loss and/or said composition for use in treating alopecia, in particular androgenetic alopecia.

TITLE: Cosmetic composition comprising niacinamide and gingerol for the treatment of hair loss

The present invention relates to the field of scalp and keratin fiber care, more particularly to the field of growth of keratin fibers, and prevention of their loss.

The present invention relates to a cosmetic composition comprising:
- at least one compound having formula (I),
- at least one gingerol, and
- optionally at least one shogaol;

wherein the mass ratio of [compound(s) having formula (I)/gingerol(s)] is less than or equal to 150, and

when said composition comprises at least one shogaol, then the mass ratio of [gingerol(s)/shogaol(s)] is greater than or equal to 1.

The invention also relates to a cosmetic treatment method comprising at least one step of applying this composition on keratin materials. The invention also relates to the non-therapeutic cosmetic use of this combination to induce and/or stimulate the growth of keratin fibers and/or impede their loss and/or to treat alopecia, in particular androgenetic alopecia.

Hair growth and renewal are mainly determined by the activity of hair follicles and their matrix environment. Their activity is cyclic and essentially includes three phases, namely the anagen phase, the catagen phase and the telogen phase.

The anagen phase (active or growth phase), which lasts several years and during which hair grows longer, is succeeded by a very short and transitory catogen phase which lasts a few weeks, followed by a telogen phase or rest phase which lasts a few months. At the end of the rest period, the hair falls out and another cycle recommences. Therefore, hair is constantly being renewed and of the approximately 150,000 individual hairs on a head of hair, approximately 10% are at rest and will be replaced in the months to come. Natural hair shedding or loss can be estimated, on average, at a few hundred individual hairs per day for a normal physiological state. This continuous physical renewal process undergoes natural changes during aging, hair becomes thinner and cycles shorter. Furthermore, various causes can result in substantial temporary or definitive hair loss. Hair loss, in particular alopecia, is essentially due to hair renewal

disturbances. These disturbances result in a first phase in cycle frequency acceleration at the cost of hair quality, and then quantity. Progressive bulb miniaturization occurs, together with isolation of said bulbs by progressive thickening of the perifollicular collagen matrix as well as of the outer sheath. Revascularization around the hair follicle is therefore made more difficult cycle after cycle. The hair recedes, getting smaller until it is merely a non-pigmented down and these phenomenon results in progressive hair thinning. The hair follicles making up a head of hair are affected in number and in average diameter. Some areas are affected preferentially, in particular on the temple or forehead hairlines in men, and in women, diffuse vertex alopecia is observed.

The term alopecia also covers a family of hair follicle disorders ultimately resulting in definitive, partial or general hair loss. It more particularly consists of androgenetic alopecia. In a large number of cases, premature hair loss occurs in genetically predisposed individuals, this consists of andro-chrono-genetic alopecia; this form of alopecia particularly concerns men. It is known, moreover, that some factors such as hormonal imbalance, physiological stress, malnutrition, can accentuate the phenomenon. Furthermore, hair loss or alteration may be linked with seasonal phenomena.

Hair density loss and hair loss are often perceived as distressing by those affected, in particular when they are still young.

Pharmacological active agents such as minoxidil, latanoprost, fluridil, spironolactone and their combinations are known.

Other products exist and belong to the field of cosmetics. Of these, mention can be made for example of aminexil® and stemoxydine®.

Nevertheless, consumers are increasingly seeking effective natural alternatives, which would delay the "hair density loss" or "excessive hair loss" process.

Furthermore, the formulation of environmentally friendly cosmetic products, i.e., the design and development of which account for environmental concerns, is becoming a major concern to help meet global challenges.

It has therefore become essential to propose more sustainable compositions to meet these environmental challenges. In this context, it is important to develop novel cosmetic compositions with a better carbon footprint, in particular by promoting the use of renewable raw materials and/or those with a good wilderness quality index and/or of natural origin, and more particularly those of plant origin, while reducing the use of compounds of petrochemical origin.

Thus, there is a need to provide combinations of natural active agents which make it possible to prevent and/or treat hair density loss effectively.

The applicant surprisingly discovered that a composition comprising at least one compound having formula (I) and at least one gingerol in precise proportions makes it possible to modulate the level of expression of a series of genes associated with the HIF-1 biological pathway. This pathway is known in the literature for its role in hair loss (F Juchaux, T Sellathurai, V Perrault, F Boirre, P Delannoy, K Bakkar, J Albaud, A Gueniche, A Cheniti, S Dal Belo, L Souverain, M Le Balch, S Commo, S Thibaut, J F Michelet. "A combination of pyridine-2, 4-dicarboxylic acid diethyl ester and resveratrol stabilizes hypoxia-inducible factor 1-alpha and improves hair density in female volunteers", Int J Cosmet Sci. 2020 Apr;42(2):167-173). Thus, the combination of at least one compound having formula (i), preferably niacinamide, or nicotinamide, or vitamin B3, with at least one gingerol, preferably in the form of extracts containing gingerols such as ginger extract, in precise proportions has advantageous properties as an active agent for inducing and/or stimulating the growth of keratin fibers such as hair, eyelashes, body hair, and eyebrows and/or impeding their loss, and in particular for treating alopecia, in particular androgenetic alopecia.

The invention therefore relates to a cosmetic composition comprising in a physiologically acceptable medium:

- at least one compound having formula (I),
- at least one gingerol, and
- optionally at least one shogaol;

wherein the mass ratio of [compound(s) having formula (I)/gingerol(s)] is less than or equal to 150, and

when said composition comprises at least one shogaol, then the mass ratio of [gingerol(s)/shogaol(s)] is greater than or equal to 1.

The present invention also relates to a cosmetic treatment method comprising at least one step of applying a cosmetic composition according to the invention on keratin materials, to induce and/or stimulate the growth of keratin fibers and/or impede their loss.

The present invention also relates to a cosmetic treatment method comprising at least one step of applying a cosmetic composition according to the invention on keratin materials, to treat alopecia, in particular androgenetic alopecia.

The invention also relates to a non-therapeutic cosmetic use of a combination of active agents comprising:

- at least one compound having formula (I),
- at least one gingerol, and
- optionally at least one shogaol;

wherein the mass ratio of [compound(s) having formula (I)/gingerol(s)] is less than or equal to 150, and

when said composition comprises at least one shogaol, then the mass ratio of [gingerol(s)/shogaol(s)] is greater than or equal to 1;

to induce and/or stimulate the growth of keratin fibers and/or impede their loss.

The invention also relates to a non-therapeutic cosmetic use of a combination of active agents comprising:

- at least one compound having formula (I),
- at least one gingerol, and
- optionally at least one shogaol;

wherein the mass ratio of [compound(s) having formula (I)/gingerol(s)] is less than or equal to 150, and

when said composition comprises at least one shogaol, then the mass ratio of [gingerol(s)/shogaol(s)] is greater than or equal to 1;

to treat alopecia, in particular androgenetic alopecia.

Definition

For the purposes of the invention, "cosmetic composition" means a composition comprising a physiologically acceptable medium, i.e. a medium compatible with the skin.

For the purposes of the invention, "keratin materials" means materials comprising keratin such as the skin, scalp and keratin fibers. In particular, the keratin materials are preferably human keratin materials.

For the purposes of the invention, "keratin fibers" means keratin fibers, preferably human, such as hair, eyelashes, body hair and/or eyebrows, preferably eyelashes and hair, more preferably hair.

For the purposes of the invention, "impede the loss of keratin fibers" means to slow down or reduce keratin fiber loss.

For the purposes of the invention, "stimulate the growth of keratin fibers" means to promote or improve the growth of existing keratin fibers, in particular to increase the length and/or diameter of existing keratin fibers and/or increase the number of keratin fibers and/or increase the density of keratin fibers.

For the purposes of the invention, "induce the growth of keratin fibers" means to promote or improve the growth of new keratin fibers, in particular keratin fiber density (through the growth of new keratin fibers).

For the purposes of the invention, "treat alopecia, in particular androgenetic alopecia" means to promote or improve the growth of new keratin fibers, or to slow down or reduce keratin fiber loss in those suffering from alopecia, in particular androgenetic alopecia.

"Mass ratio of [compound(s) having formula (I)/gingerol(s)]" means the mass ratio of all the compounds having formula (I) present in the composition or in the combination of active agents with respect to all the gingerols present (or total gingerols) in the composition or in the combination of active agents. It is calculated by dividing the sum of the masses of all the compounds having formula (I) by the sum of the masses of all the gingerols present.

"Mass ratio of [gingerol(s)/shogaol(s)]" means the mass ratio of all the gingerols present in the composition or in the combination of active agents with respect to all the shogaols present in the composition or in the combination of active agents. It is calculated by dividing the sum of the masses of all the gingerols present by the sum of the masses of all the shogaols present.

"Alkyl" means a monovalent linear or branched saturated hydrocarbon chain.

C1-C4 alkyl means an alkyl radical comprising 1 to 4 carbon ataoms such as methyl, ethyl, propyl, isopropyl, butyl, isobutyl, tetriobutyl, and preferably methyl or ethyl.

C1-C4 (hydroxy)alkyl means 1-C4 alkyl radical substituted by a hydroxy radical.

"Heterocycle" means a cyclic radical of which at least one of the members denotes a heteroatom preferably chosen from N, O, S, more preferably N.

"Salt" means an addition salt with an organic or mineral acid or base. The addition salts with an acid are in particular chosen from addition salts with acids such as hydrochloric acid, hydrobromic acid, sulfuric acid, citric acid, succinic acid, tartaric acid, lactic acid, tosylic acid, benzenesulfonic acid, phosphoric acid or acetic acid. The addition salts with a base

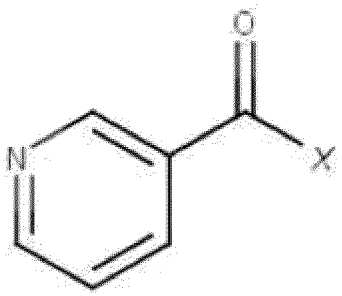
are in particular chosen from addition salts with bases such as alkali metal hydroxides, alkaline earth metal hydroxides, ammonia, amines or alkanolamines.

Composition

The composition according to the invention contains at least one compound having formula (i).

For the purposes of the invention, the compositions having formula (I) have the following structure, as well as their addition salts:

[Chem 1]



(I)

wherein

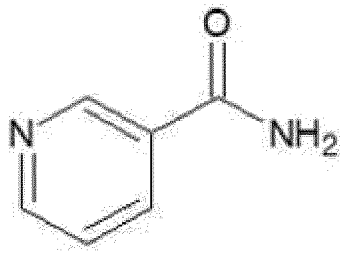
- *X* is the group OR or the group NRaRb
  - Ra and Rb denote independently a hydrogen atom or a C1-C4 alkyl radical such as methyl, or Ra and Rb can form together with the nitrogen atom carrying them a 5- or 6-member heterocycle, said heterocycle being optionally substituted by one or more C1-C4 (hydroxy)alkyl radicals or one or more hydroxy radicals;
  - R denotes a hydrogen atom or a C1-C4 alkyl radical such as ethyl or a C1-C4 (hydroxy)alkyl radical.

Preferably, Ra and Rb denote independently a hydrogen atom or a C1-C4 alkyl radical such as methyl, more preferably Ra and Rb denote a hydrogen atom.

Preferably, R denotes a hydrogen atom.

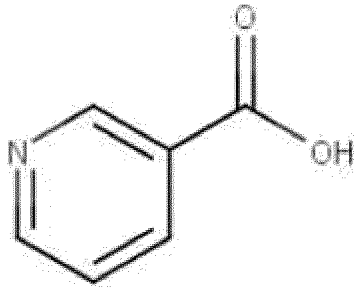
According to one preferred embodiment, the compounds having formula (I) are chosen from the following compounds (II) and (III), mixtures thereof, as well as their salts.

[Chem 2]



(II)

[Chem 3]



(III)

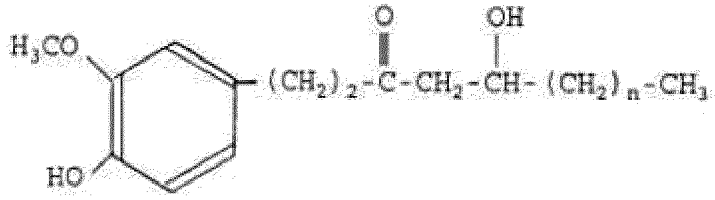
According to one preferred embodiment, the at least one compound having formula (I) comprises the compound (II) named niacinamide or (3-pyridinecarboxamide) also known as nicotinamide. According to one preferred embodiment, the at least one compound having formula (I) is the compound (II) named niacinamide or (3-pyridinecarboxamide) also known as nicotinamide.

Mention can be made for example of the product Niacinamide PC® marketed by DSM NUTRITIONAL PRODUCTS.

Preferably, the composition comprises from 1% to 5% by weight of compound(s) having formula (I) with respect to the total weight of the composition, preferably from 1.5% to 4.5% by weight, preferably from 2% to 4% by weight, with respect to the total weight of the composition.

The composition according to the invention comprises at least one gingerol. Gingerols are compounds of the arylalkanol family complying with the following general formula (IV):

[Chem 4]



(IV)

They are found in plants of the Zingiberaceae family.

According to the invention, gingerols complying with general formula (IV) mentioned hereinabove wherein n is equal to 2, 4, 6 or 8 and which are known under their respective names of [4]-gingerol, [6]-gingerol, [8]-gingerol and [10]-gingerol are preferably used.

Preferably, said at least one gingerol is a mixture of gingerols.

Preferably, said at least one gingerol is a mixture of gingerols, said mixture comprising at least [6]-gingerol.

Preferably, said at least one gingerol is a mixture of gingerols, said mixture comprising at least [6]-gingerol at a concentration of at least 50% by weight with respect to the total weight of the gingerol mixture.

Preferably, the composition comprises a ginger extract comprising said at least one gingerol, wherein the gingerol(s) is(are) present in the ginger extract at a concentration ranging from 10% to 35% by weight with respect to the total weight of the ginger extract, preferably 12 to 32% by weight, more preferably from 14 to 30% by weight with respect to the total weight of the ginger extract.

Preferably, the composition comprises a ginger extract comprising said at least one gingerol, said at least one gingerol being a mixture of gingerols comprising at least [6]-gingerol present in the ginger extract at a concentration of at least 8% by weight with respect to the total weight of the ginger extract, preferably at least 10% by weight, more preferably at least 13% by weight, more preferably at least 15% by weight with respect to the total weight of the ginger extract.

Preferably, said at least one gingerol is chosen from [6]-gingerol, [8]-gingerol, [10]-gingerol and mixtures thereof.

Preferably, said at least one gingerol is present in the composition according to the invention at a content ranging from 0.00001% to 1% by weight of total gingerols with respect to the total weight of the composition, preferably from 0.0001% to 0.5%, more preferably

0.0002% to 0.1% by weight of total gingerols with respect to the total weight of the composition.

Preferably, the composition comprises a ginger extract comprising said at least one gingerol wherein:

- the concentration of [6]-gingerol is between 5 and 20% by weight with respect to the weight of the extract, and more preferably between 12.5 and 17.5% by weight with respect to the weight of the extract; and/or
- the concentration of [8]-gingerol is between 1 and 5% by weight with respect to the weight of the extract, and more preferably between 2 and 4% by weight with respect to the weight of the extract; and/or
- the concentration of [10]-gingerol is between 1 and 10% by weight with respect to the weight of the extract, and more preferably between 3 and 7% by weight with respect to the weight of the extract.

Said at least one gingerol can be in the form of extracts, by any extraction method known per se, of plants belonging to the Zingiberaceae family and, more particularly, of those belonging to the *Zingiber* genus and in particular to the *Zingiber officinalis* species (commonly referred to as ginger). More particularly, said at least one gingerol can be in the form of root extracts of these plants (also referred to here as ginger root extract).

In particular, the ginger root extract can be in the form of ground product, powder or liquid, it is preferably in liquid form.

The ginger root extract can in particular be obtained by supercritical CO_2 extraction from ginger root fragments, example from ginger root powder. The ginger root extract used is preferably an extract obtained by supercritical CO_2 extraction such as that sold under the name GINGER CO2 by FLAVEX.

In the case where said at least one gingerol is in the form of ginger root extract, said extract is then present preferably at a content ranging from 0.00003 to 1% by weight, preferably from 0.0001 to 0.5% by weight, more preferably 0.001 to 0.3% by weight, with respect to the total weight of the composition.

Said at least one gingerol can also be obtained by chemical synthesis, for example according to the methods described by BANNO and MUKAIYAMA, Bull. Chem. Soc. Japan, 49(5), 1453-1454 (1976). Said at least one gingerol can also be obtained by purification or

enrichment of natural plant extracts such as extracts of plants belonging to the Zingiberaceae family, in particular those belonging to the *Zingiber* genus, more particularly to the *Zingiber officinalis* species

In particular, the applicant discovered a synergistic effect between:

- said at least one compound having formula (I), preferably chosen from the compounds having formula (II) and (III) and mixtures thereof, more preferably niacinamide, and
- said at least one gingerol,

could be obtained when they are used in a particular ratio.

Thus, according to the invention, the mass ratio of [compound(s) having formula (I)/gingerol(s)] in the composition is less than or equal to 150, preferably less than or equal to 140, more preferably less than 130, advantageously it is between 0.01 and 150, preferably between 0.1 and 140, and more preferably between 0.1 and 130.

According to one embodiment, the mass ratio of [compound(s) having formula (II) and/or (III)/gingerol(s)], in the composition is less than or equal to 150, preferably less than or equal to 140, more preferably less than 130, advantageously it is between 0.01 and 150, preferably between 0.1 and 140, and more preferably between 0.1 and 130.

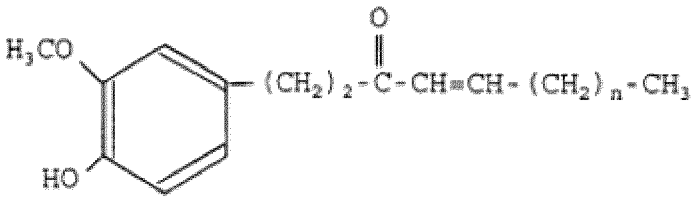
According to one embodiment, the mass ratio of [compound(s) having formula (I)/[6]-gingerol] in the composition is less than or equal to 250, preferably less than or equal to 200, more preferably less than 195, advantageously it is between 0.01 and 250, preferably between 0.1 and 200, and more preferably between 0.1 and 195.

According to one embodiment, the mass ratio of [compound(s) having formula (II) and/or (III)/[6]-gingerol] in the composition is less than or equal to 250, preferably less than or equal to 200, more preferably less than 195, advantageously it is between 0.01 and 250, preferably between 0.1 and 200, and more preferably between 0.1 and 195.

In one embodiment of the invention, the mass ratio of [compound(s) having formula (I)/ginger extract] in the composition is less than or equal to 40, less than or equal to 35, preferably less than or equal to 30, advantageously it is between 0.01 and 35, preferably between 0.03 and 30.

The composition according to the invention optionally comprises at least one shogaol. Shogaols are compounds of the arylalkanone family complying with the following general formula (V):

[Chem 5]



(V)

They are found in plants of the Zingiberaceae family.

According to the invention, shogaols complying with general formula (V) mentioned hereinabove wherein n is equal to 1, 2, 4, 6 or 8 and which are known respectively as [3]-shogaol, [4]-shogaol, [6]-shogaol, [8]-shogaol and [10]-shogaol are preferably used. Preferably, said at least one shogaol is chosen from [6]-shogaol, [8]-shogaol, [10]-shogaol and mixtures thereof.

Shogaols can be produced when ginger is dried or cooked. Shogaols can be extracted from *Zingiberaceae* roots by identical methods to those used for gingerol extraction.

Preferably, said at least one shogaol is present in the composition according to the invention at a content less than 0.02% by weight of total shogaols with respect to the total weight of the composition, preferably less than 0.01%, more preferably less than 0.005%, preferably less than 0.0002%, more particularly less than 0.0001% by weight of total shogaols with respect to the total weight of the composition.

Preferably, the composition comprises a ginger extract comprising said at least one shogaol wherein:

- the concentration of [6]-shogaol is between 0.1 and 5% by weight with respect to the weight of the extract, and more preferably between 1.5 and 2.5% by weight with respect to the weight of the extract; and/or
- the concentration of [8]-shogaol is between 0.1 and 3% by weight with respect to the weight of the extract, and more preferably between 0.3 and 0.5% by weight with respect to the weight of the extract; and/or

- the concentration of [10]-shogaol is between 0.01 and 1% by weight with respect to the weight of the extract, and more preferably between 0.08 and 0.2% by weight with respect to the weight of the extract.

Preferably, said at least one shogaol can be in the form of an extract of ginger (*Zingiber officinale*), preferably a ginger root extract. Said at least one shogaol can be in the form of extracts, by any extraction method known per se, of plants belonging to the Zingiberaceae family and, more particularly, of those belonging to the *Zingiber* genus and in particular to the *Zingiber officinalis* species (commonly referred to as ginger). More particularly, said at least one shogaol can be in the form of root extracts of these plants (also referred to here as ginger root extract).

In particular, the ginger root extract can be in the form of ground product, powder or liquid, it is preferably in liquid form.

The ginger root extract can in particular be obtained by supercritical CO_2 extraction from ginger root fragments, example from ginger root powder. The ginger root extract used is preferably an extract obtained by supercritical CO_2 extraction such as that sold under the name GINGER CO2 by FLAVEX.

In one embodiment of the invention, the composition comprises a ginger extract comprising said at least one gingerol and said at least one shogaol. Preferably, this ginger extract, preferably of ginger root, is composed of:

- 10% to 35% of total gingerols with respect to the total weight of the extract, preferably from 12% to 32%, preferably 14-30% by weight of total gingerols with respect to the total weight of the extract;
- less than 15% of total shogaols with respect to the total weight of the extract, preferably less than 10%, preferably less than 5% by weight of total shogaols with respect to the total weight of the extract.

Preferably, the composition comprises a ginger extract comprising said at least one gingerol and said at least one shogaol wherein:

- the concentration of [6]-gingerol is between 5 and 20% by weight with respect to the weight of the extract, and more preferably between 12.5 and 17.5%; and/or
- the concentration of [8]-gingerol is between 1 and 5% by weight with respect to the weight of the extract, and more preferably between 2 and 4%; and/or

- the concentration of [10]-gingerol is between 1 and 10% by weight with respect to the weight of the extract and more preferably between 3 and 7%; and/or
- the concentration of [6]-shogaol is between 0.1 and 5% by weight with respect to the weight of the extract, and more preferably between 1.5 and 2.5%; and/or
- the concentration of [8]-shogaol is between 0.1 and 3% by weight with respect to the weight of the extract, and more preferably between 0.3 and 0.5%; and/or
- the concentration of [10]-shogaol is between 0.01 and 1% by weight with respect to the weight of the extract and more preferably between 0.08 and 0.2%.

In the embodiment of the invention where the composition comprises a ginger extract comprising said at least one gingerol and said at least one shogaol, the extract can be a ginger root extract present in the composition at a content ranging from 0.02 to 1% by weight, preferably from 0.03 to 0.5% by weight, more preferably from 0.05 to 0.3% by weight, with respect to the total weight of the composition. The ginger root extract used is preferably an extract obtained by supercritical CO_2 extraction such as that sold under the name GINGER CO2 by FLAVEX.

The applicant also discovered that when the composition according to the invention comprises at least one shogaol, the effect of said composition could be decreased if the mass ratio between gingerols and shogaols is strictly less than 1.

Thus according to the invention, when said composition comprises at least one shogaol, then the mass ratio of [gingerol(s)/shogaol(s)] is greater than or equal to 1, preferably greater than 3, more preferably greater than 6, even more preferably greater than 9. In one preferred embodiment, this ratio is between 1 and 15, preferably between 5 and 12, more preferably between 8 and 10.

According to one embodiment of the invention, the mass ratio of [6], and [8], and [10]-gingerol to [6], and [8], and [10]-shogaol is greater than or equal to 3, preferably greater than 3, more preferably greater than 6, even more preferably greater than 9. In one preferred embodiment, this ratio is between 3 and 15, preferably between 5 and 12, more preferably between 8 and 10.

In one embodiment, the composition according to the invention does not comprise other active agents than:

- at least one compound having formula (I), preferably at least one compound having formula (II) and/or (III), more preferably a compound having formula (II),
- at least one gingerol, and
- at least one shogaol.

The composition according to the invention preferably contains a physiologically acceptable medium.

This physiologically acceptable medium can comprise water and optionally one or more physiologically acceptable organic solvents chosen for example from lower alcohols having from 1 to 8 carbon atoms and in particular 1 to 6 carbon atoms, such as ethanol, isopropanol, propanol, butanol; polyethylene glycols having from 6 to 80 ethylene oxides; polyols such as propylene glycol, isoprene glycol, butylene glycol, glycerin, sorbitol, 1,3-propanediol.

It can also be an anhydrous medium containing oils and/or fats other than oils.

When the physiologically acceptable medium is an aqueous medium, it has a pH compatible with the skin, ranging preferably from 3 to 8 and more preferably from 4 to 7.

When the composition includes an aqueous or hydroalcoholic medium, it is possible to add a fatty (or oily) phase to this medium.

The composition according to the invention is in particular a composition intended for topical application on the scalp and/or keratin fibers.

The composition according to the invention can also comprise one or more additional compounds chosen in particular from surfactants, preferably chosen from non-ionic, anionic, cationic and amphoteric surfactants, conditioning agents preferably chosen from cationic polymers, silicones, optionally polymeric thickening agents, natural or synthetic, UV filters, fillers such as nacres, titanium dioxide, resins and clays, perfumes, peptizers, vitamins different from vitamin B3, preservatives, acidic agents, alkaline agents, additional active agents different from the compounds according to the invention intended to further improve the activity on regrowth and/or slowing down hair loss, and already described for this activity, such as nicotinic acid esters, of which in particular tocopherol nicotinate, benzyl nicotinate and C1-C6 alkyl nicotinates such as methyl or hexyl nicotinates; agents promoting hair regrowth chosen from pyrimidine 3-oxide derivatives such as 2,4-diaminopyrimidine-3-N-oxide (Aminexil), pyridine-dicarboxylate derivatives or one of its salts such as those described in FR2838336 such as pyridine-2,4-dicarboxylate dimethyl ester, and/or pyridine-2,4-dicarboxylate diethyl ester; and a mixture of these compounds.

Thus, according to an embodiment, the composition further comprises one or more agents promoting hair regrowth, these agents promoting hair regrowth being selected from:

- pyrimidine 3-oxide derivatives such as 2,4-diaminopyrimidine-3-N-oxide,
- pyridine-dicarboxylate derivatives such as pyridine-2,4-dicarboxylic acid diethyl ester; and
- a mixture thereof.

According to a preferred embodiment, the composition according to the invention further comprises 2,4-diaminopyrimidine-3-N-oxide (Aminexil), and/or pyridine-2,4-dicarboxylic acid diethyl ester (stemoxydine).

The additional compounds hereinabove can each be present in a quantity varying from 0.01% to 20% by weight with respect to the total weight of the composition.

The composition according to the invention is intended for cosmetic use by topical application on the scalp and/or keratin fibers, and more especially on the scalp, hair and eyelashes, body hair, eyebrows.

According to the application method, this composition can be in any dosage forms normally used in the field of cosmetics, such as lotion, serum, milk, cream, gel, unguent, ointment, powder, balm, patch, impregnated pad, soap, bar, mousse. It can be formulated in the form of emulsion, such as a direct oil-in-water emulsion or an invert water-in-oil emulsion.

For topical application on the scalp and/or keratin fibers, the composition can take the form in particular of an aqueous or hydroalcoholic solution or suspension, an emulsion or dispersion of liquid or semi-liquid consistency obtained by dispersing a fatty phase in an aqueous phase (O/W) or conversely (W/O), a dispersion or emulsion of soft consistency, an aqueous or hydroalcoholic gel, or microcapsules or microparticles, or ionic and/or non-ionic type vesicular dispersions.

The composition can also be in the form of a mousse or in the form of an aerosol composition also comprising a pressurized propellant.

Preferably, for topical application on the scalp and/or keratin fibers, in particular the scalp or hair, the composition can be in the form of a hair lotion, a shampoo, a conditioner, a hairstyling product (hairspray, hair setting product, styling gel), a hair mask, a cream or a foaming gel for cleaning hair.

According to one preferred embodiment, the composition according to the invention is in the form of a cream or lotion, shampoo or conditioner.

Method

The present invention also relates to a non-therapeutic cosmetic treatment method comprising applying the composition described hereinabove on keratin materials, to induce and/or stimulate the growth of keratin fibers and/or impede their loss.

The present invention also relates to a non-therapeutic cosmetic treatment method comprising applying the composition described hereinabove on keratin materials, to treat alopecia, in particular androgenetic alopecia.

In particular, the composition described hereinabove is applied to a subject in a normal physiological state, i.e. not suffering from any pathology; alternatively to a subject not suffering from any dermatological pathology, even more preferably to a subject not suffering from any pathology of the scalp.

By "subject", it should be understood herein a human being, preferably a human.

In particular, the method comprises applying the composition on the scalp and/or keratin fibers, then, optionally, rinsing, after setting the composition from 1 minute to 30 minutes.

Preferably, the cosmetic composition is not rinsed.

Use

The present invention relates to the non-therapeutic cosmetic use of a combination of active agents comprising:

- at least one compound having formula (I) as described hereinabove,
- at least one gingerol, and
- optionally at least one shogaol;

wherein the mass ratio of [compound having formula (I)/gingerol(s)] is less than or equal to 150, and

when said composition comprises at least one shogaol, then the mass ratio of [gingerol(s)/shogaol(s)] is greater than or equal to 1;

to induce and/or stimulate the growth of keratin fibers and/or impede their loss.

The present invention also relates to the non-therapeutic cosmetic use of a combination of active agents comprising:

- at least one compound having formula (I) as described hereinabove,
- at least one gingerol, and

- optionally at least one shogaol;

wherein the mass ratio of [compound having formula (I)/gingerol] is less than or equal to 150, and

when said composition comprises at least one shogaol, then the mass ratio of [gingerol(s)/shogaol(s)] is greater than or equal to 1;

to treat alopecia, in particular androgenetic alopecia.

Preferably, the combination of active agents used according to the invention comprises the same active agents in the same concentrations and/or proportions as described hereinabove for the composition according to the invention.

The present invention relates to the non-therapeutic cosmetic use of a composition according to the invention to induce and/or stimulate the growth of keratin fibers and/or impede their loss.

The present invention also relates to the non-therapeutic cosmetic use of a composition according to the invention to treat alopecia, in particular androgenetic alopecia.

In particular, the composition described hereinabove is applied to a subject in a normal physiological state, i.e. not suffering from any pathology; alternatively to a subject not suffering from any dermatological pathology, even more preferably to a subject having not suffering from any pathology of the scalp.

By “subject”, it should be understood herein a human being, preferably a human.

The invention will become more apparent upon reading the following description, given solely as a non-limiting example, and made with reference to the drawings wherein:

Moreover, the expression "at least one" used in the present description is equivalent to the expression "one or more".

Figure:

[Fig 1] Figure 1 shows a bar graph representing the HIF-1 pathway activation level according to the different niacinamide/ginger root extract mass ratios tested.

Example:

<u>Evaluation of HIF-1 pathway activation, for an anti-hair loss application</u>

The purpose of this study is to compare the efficacy of the Niacinamide-Ginger root extract combination to the efficacy of both compounds when they are separated on HIF-1 pathway activation. This activation is measured thanks to monitoring of the expression level of genes under the control HIF-1alpha (Hypoxia Induced Factor 1 alpha) factor by quantitative RT-PCR.

The genes studied are: EGLN3, BNIP3, CA9, VEGFA.

The tests were performed on human keratinocytes in culture, inoculated on 48-well plates, coated with bovine collagen I. The plates were prepared according to the following procedure: the solution of bovine collagen I at 0.1 mg/ml was prepared by dilution in a phosphate buffered saline (PBS) bovine collagen I solution. Each well was then submerged with 1 ml of this dilution, which was left at the bottom of the wells for 1 hour at 37°C. At the end of incubation, the collagen solution was removed and the wells were rinsed twice with 1 ml of PBS. The plates were then stored at 4°C until use. The tests were performed on primary human keratinocytes at a rate of 23,800 cells/cm^2 of wells covered with bovine collagen I as explained hereinabove, followed by a culture for 72 hours in the presence of 500 µL of KGM medium, supplemented with: 0.1% by weight of commercial gentamicin sulfate/amphotericin mixture, 0.4% by weight of bovine pituitary extract, 0.1% by weight of insulin, 0.1% by weight of hydrocortisone and 0.1% by weight of epidermal growth factor (or human recombinant EGF), at 37°C in an atmosphere saturated with water and containing 5% CO_2.

The cells were then treated with the niacinamide and Ginger root extract compounds (containing 15.5% [6]-Gingerol, 3.6% [8]-Gingerol and 5.5% [10]-Gingerol; 2.1% [6]-shogaol, 0.46% [8]-shogaol and 0.17% [10]-shogaol) at the highest non-cytotoxic concentrations (0.2 mg/mL and 0.01 mg/mL respectively), for 48 hours under normoxia (21% oxygen). Following this culture and this treatment, the cell lawns was washed with a phosphate buffered saline (or PBS) solution then lyzed using a lysis buffer. The RNA was then extracted using the RNeasy isolation kit and Qiacubestation. The quantity and quality of the RNA were tested using the LabChip® GX Bioanalyzer from Perkin-Elmer before performing reverse transcription (RT) using the Qiagen kit and according to recommendations. The cDNA obtained following the RT was then amplified by real-time PCR quantitative calculations using a specific kit and a thermocycler. The PCRs were carried out in triplicate (n=3).

Priming was carried out using specific standard primers, and the SYBR Green brand fluorescent probe. The PCR was carried out in three phases:

- denaturing phase for 10 minutes at 95°C,
- amplification phase made up of 45 cycles comprising a denaturing step of 30 seconds at 95°C, a hybridization step of 30 seconds at 60°C, and an elongation step at 72°C for 30 seconds,
- fusion phase to ensure hybridization quality. The incorporation of SYBR Green in the amplified DNA was measured continuously during the amplification cycles.

These measurements make it possible to obtain fluorescence intensity curves according to the PCR cycles and thus evaluate the relative expression of each marker using the cycle thresholds (Ct), corresponding to the number of cycles required to detect a fluorescence level correctly. For each marker and for each condition, the relative expression (RE) value was standardized with respect to the expression of the gene reference RPL 13. The expression of each gene is standardized by that of the "stable reference gene" (or "household gene" RPL 13A, ribosomal gene).

The results are expressed by the "fold change" (Fc) of gene expression with respect to the control condition (without treatment).

[Table 1] Table 1

Name	Abbreviation	Registration number
Carbonic anhydrase IX	CA9	NM_001216
BCL2/adenovirus E1B 19 kDa-interacting protein	BN1P3	NM_004052
Prolyl hydroxylase	EGLN3 (or PHD3)	NM_022073
Vascular Endothelial Growth Factor	VEGFA	NP_001165097
Ribosomal protein L13	RPL13	NM_000977

RESULTS AND CONCLUSIONS

1. **Synergistic action of the two active agents Niacinamide – ginger extract comprising gingerols**

All of the results are expressed via the modulation factor (fold change) with respect to the untreated control after standardizing the relative expression with respect to the expression of a household gene (RPL13). The expression of a gene is considered to be stimulated when it is multiplied at least by 1.5.

Table 2 shows the effects of the niacinamide and Ginger Extract compounds, alone and in combination, on the example of a selection of genes in relation to described effects of hypoxia for an anti-hair loss benefit.

[Table 2] Table 2

	EGLN3	BNIP3	CA9	VEGF
Niacinamide 0.3 mg/mL in DMSO	2.13	1.34	1.96	0.89
Ginger root extract 0.01 mg/mL in DMSO	1.58	0.93	1.51	1.78
COMBINATION of the 2 compounds Niacinamide 0.3 mg/mL + Ginger root extract 0.01 mg/mL in DMSO	4.09	4.16	6.86	2.34

The results show a synergistic effect of the Niacinamide and ginger root extract combination. Indeed, treated with this combination, all the genes are expressed with a modulation factor substantially greater than 1.5 with respect to the control, which confirms the significant effect of this combination, which is not the case for the raw materials tested separately. The Niacinamide-Ginger root extract combination induces a significant stimulation of the expression of the EGLN3, BNIP3, CA9 and VEGF genes which are described in the literature as being associated with the HIF-1 biological pathway (Pouyssegur J et al., MEDECINE/SCIENCES 2002; 18: 70-8). When the HIF-1 transcription factor is stabilized (in hypoxic medium or following a treatment allowing its activation), it is translocated in the nucleus of the cells and activates a large number of genes, of which EGLN3, BNIP3 and CA9 and VEGF, associated with the regeneration of tissues such as the skin and hair.

The stimulation of the expression of these genes in the presence of the Niacinamide-Ginger root extract combination is greater than the addition of the effects of two compounds applied separately.

2. Mass ratios of niacinamide and gingerol concentrations to activate HIF-1

Table 3 hereinafter and Figure 1 show the different Niacinamide and Ginger root extract concentration ratios tested and their effects on HIF-1 pathway activation.

[Table 3] Table 3

NIACINAMIDE (g/100g) %	Ginger root extract (g/100g) %	Total gingerols (g/100g)	MASS RATIO of Niacinamide / Ginger root extract	MASS RATIO of Niacinamide / total gingerols	Mean gene expression modulation factor EGLN3, BNIP3, CA9 and VEGFA.	standard deviation
0.000033	0.001	0.000246	0.033	0.134	2.38	na
0.0001	0.00025	0.0000615	0.4	1.63	2.78	na
0.001	0.001	0.000246	1	4.07	1.58	na
0.0025	0.001	0.000246	2.5	10.16	2.69	0.39
0.0025	0.001	0.000246	2.5	10.16		
0.0025	0.001	0.000246	2.5	10.16		
0.0025	0.001	0.000246	2.5	10.16		
0.00025	0.0001	0.0000246	2.5	10.16		
0.0025	0.0005	0.000123	5	20.33	5.00	0.45
0.005	0.001	0.000246	5	20.33		
0.005	0.001	0.000246	5	20.33		
0.005	0.001	0.000246	5	20.33		
0.005	0.001	0.000246	5	20.33		
0.005	0.001	0.000246	5	20.33		
0.005	0.0005	0.000123	10	40.65	2.91	na
0.02	0.001	0.000246	20	81.30	20.00	0.84
0.02	0.001	0.000246	20	81.30		
0.02	0.001	0.000246	20	81.30		
0.02	0.001	0.000246	20	81.30		
0.02	0.001	0.000246	20	81.30		
0.02	0.001	0.000246	20	81.30		
0.02	0.001	0.000246	20	81.30		
0.02	0.001	0.000246	20	81.30		
0.015	0.0005	0.000123	30	121.95	2.45	0.01
0.001	0.000033	0.00000812	30	121.95		
0.02	0.0005	0.000123	40	162.60	1.27	na
0.0005	0.00001	0.00000246	50	203.25	1.10	0.40
0.02	0.0004	0.0000984	50	203.25		

The results show that Niacinamide and ginger root extract concentration ratios less than or equal to 30:1 are effective for stimulating the expression of genes in relation with the effects described of hypoxia for an anti-hair loss benefit: Fold Change > 1.5.

When the concentration ratio is greater than 30:1, the combination is no longer effective.

3. Demonstration of the active agents carrying efficacy in Ginger root extract: Gingerols

As detailed in the analysis of ingredients hereinafter, the ginger root extracts used in the examples according to the invention contain on average 24.6% gingerols, and in particular 15.5% [6]-gingerol, 3.6% [8]-gingerol and 5.5% [10]-gingerol.

Table 4 shows the comparison of HIF-1 pathway activation by the implementation of the protocol as detailed in point 1, between the Niacinamide-Ginger root extract (at a ratio of 30:1 and containing 24.6% gingerols) and Niacinamide-Gingerol (at a gingerol concentration corresponding to 24.6% contained in the ginger extract) combinations.

[Table 4] Table 4

TESTED COMBINATIONS (mg/ml)	TESTED COMBINATIONS (g PER 100g)	HIF-1 ACTIVATION (Fold Change)	Standard deviation
Niacinamide 0.3 mg/mL + Ginger root extract 0.01 mg/mL in DMSO	Niacinamide 0.03% + Ginger extract 0.001% i.e. 0.000246% total gingerols in DMSO (niacinamide / gingerol ratio = 121.95)	3.1	0.488
Niacinamide 0.3mg/mL + [6]-Gingerol (0.00155 mg/mL) + [8]-Gingerol (0.00036 mg/mL) + [10]-Gingerol (0.00055 mg/mL) in DMSO	Niacinamide 0.03% + [6]-Gingerol (0.000155%) + [8]-Gingerol (0.000036%) + [10]-Gingerol (0.000055%) i.e. 0.000246% total gingerols in DMSO (niacinamide / gingerol ratio = 121.95)	3.0	0.2

The efficacy is identical with both combinations. These results show that the activity of ginger root extract for activating the HIF-1 pathway is carried by gingerols.

4. Mass ratios of gingerols/shogaols for activating HIF-1

The Ginger root extract can also contain Shogaols: [6]-Shogaol, [8]-Shogaol and [10]-Shogaol.

Table 5 shows the comparison of HIF-1 pathway activation by the implementation of the protocol as detailed in point 1 hereinabove, between the Niacinamide-gingerols and Niacinamide-gingerols-shogaols combination at different [gingerol(s)/shogaol(s)] ratios. When the [gingerol(s)/shogaol(s)] ratio is strictly greater than 1 (0.90), the activity carried by the niacinamide-gingerol(s) combination is degraded. Thus, it is observed that, in the presence of shogaol(s), it is necessary for the [gingerol(s)/shogaol(s)] ratio to be greater than or equal to 1 to obtain maintained HIF-1 pathway activation efficacy.

[Table 5] Table 5

TESTED COMBINATIONS (mg/ml)	TESTED COMBINATIONS (g per 100 g)	Fold Change	Standard deviation
Niacinamide 0.3 mg/mL + [6]-Gingerol (0.00155 mg/mL) + [8]-Gingerol (0.00036 mg/mL) + [10]-Gingerol (0.00055 mg/mL) in DMSO	Niacinamide 0.03% + [6]-Gingerol (0.000155%) + [8]-Gingerol (0.000036%) + [10]-Gingerol (0.000055%) in DMSO i.e. 0.000246% total gingerols (niacinamide / gingerol mass ratio = 121.95)	4.09	1.1
Niacinamide 0.3 mg/mL + [6]-Gingerol (0.00155 mg/mL) + [8]-Gingerol (0.00036 mg/mL) + [10]-Gingerol (0.00055 mg/mL) +	Niacinamide 0.03% + [6]-Gingerol (0.000155%) + [8]-Gingerol (0.000036%) + [10]-Gingerol (0.000055%)	3.8	0.8

[6]-Shogaol (0.00021 mg/mL) + [8]-Shogaol (0.000046 mg/mL) + [10]-Shogaol (0.000017 mg/mL) in DMSO	i.e. 0.000246% total gingerols + [6]-Shogaol (0.000021%) + [8]-Shogaol (0.0000046%) + [10]-Shogaol (0.0000017%) i.e. 0.0000273% total shogaols in DMSO (niacinamide / gingerols mass ratio = 121. 95 gingerols/shogaols mass ratio = 9.01)		
Niacinamide 0.3 mg/mL + [6]-Gingerol (0.00155 mg/mL) + [8]-Gingerol (0.00036 mg/mL) + [10]-Gingerol (0.00055 mg/mL) + [6]-Shogaol (0.0021 mg/mL) + [8]-Shogaol (0.00046 mg/mL) + [10]-Shogaol (0.00017 mg/mL) in DMSO	Niacinamide 0.03% + [6]-Gingerol (0.000155%) + [8]-Gingerol (0.000036%) + [10]-Gingerol (0.000055%) i.e. 0.000246% total gingerols + [6]-Shogaol (0.00021%) + [8]-Shogaol (0.000046%) + [10]-Shogaol (0.000017%) i.e. 0.000273% total shogaols in DMSO	0.22	0.04

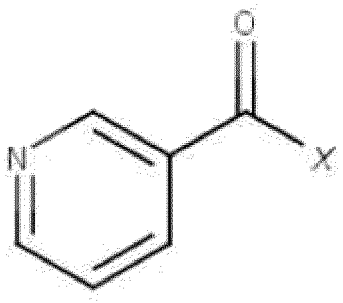
	(niacinamide / gingerols mass ratio = 121.95 and gingerols/shogaols mass ratio = 0.90)		

CLAIMS

1. Cosmetic composition comprising in a physiologically acceptable medium:

- at least one compound having formula (I),

[Chem 1]



(I)

wherein

- *X* is the group OR or the group NRaRb
- Ra and Rb denote independently a hydrogen atom or a C1-C4 alkyl radical such as methyl, or Ra and Rb can form together with the nitrogen atom carrying them a 5- or 6-member heterocycle, said heterocycle being optionally substituted by one or more C1-C4 (hydroxy)alkyl radicals or one or more hydroxy radicals;
- R denotes a hydrogen atom or a C1-C4 alkyl radical such as ethyl or a C1-C4 (hydroxyl)alkyl radical,

- at least one gingerol, and
- optionally at least one shogaol;

wherein the mass ratio of [compound(s) having formula (I)/gingerol(s)] is less than or equal to 150, and

when said composition comprises at least one shogaol, then the mass ratio of [gingerol(s)/shogaol(s)] is greater than or equal to 1.

2. Composition according to claim 1, wherein said at least one gingerol is chosen from: [6]-gingerol, [8] gingerol and [10] gingerol.

3. Composition according to claim 1 or 2, wherein said at least one gingerol and/or said at least one shogaol is in the form of a ginger extract.

4. Composition according to claim 3, wherein the mass ratio of [compound(s) having formula (I)/ginger extract] is less than or equal to 40.

5. Composition according to any one of claims 1 to 4, wherein said at least one compound having formula (I), comprises niacinamide.

6. Composition according to any one of claims 1 to 5, further comprising one or more agents promoting hair regrowth, chosen from :

- pyrimidine 3-oxide derivatives such as 2,4-diaminopyrimidine-3-N-oxide,
- pyridine-dicarboxylate derivatives such as pyridine-2,4-dicarboxylic acid diethyl ester; and
- a mixture thereof.

7. Composition according to any one of claims 1 to 6, wherein the mass ratio of [compound(s) having formula (I)/gingerol(s)] in the composition is less than 130, advantageously between 0.1 and 130.

8. Cosmetic treatment method comprising at least one step of applying a cosmetic composition according to any one of claims 1 to 7 on keratin materials, to induce and/or stimulate the growth of keratin fibers and/or impede their loss.

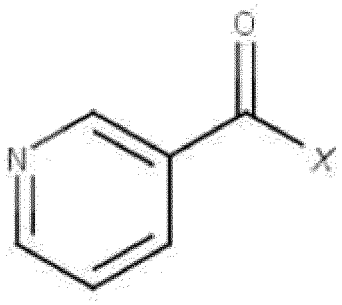
9. Cosmetic treatment method comprising at least one step of applying a cosmetic composition according to any one of claims 1 to 7 on keratin materials, to treat alopecia, in particular androgenetic alopecia.

10. Method according to any one of claims 8 to 9, wherein the keratin fibers are chosen from hair, eyelashes, body hair, and/or eyebrows.

11. Non-therapeutic cosmetic use of a combination of active agents comprising:

- at least one compound having formula (I),

[Chem 1]



(I)

wherein

- *X* is the group OR or the group NRaRb
- Ra and Rb denote independently a hydrogen atom or a C1-C4 alkyl radical such as methyl, or Ra and Rb can form together with the nitrogen atom carrying them a 5- or 6-member heterocycle, said heterocycle being optionally substituted by one or more C1-C4 (hydroxy)alkyl radicals or one or more hydroxy radicals;
- R denotes a hydrogen atom or a C1-C4 alkyl radical such as ethyl or a C1-C4 (hydroxy)alkyl radical,

- at least one gingerol, and
- optionally at least one shogaol;

wherein the mass ratio of [compound(s) having formula (I)/gingerol(s)] is less than or equal to 150, and

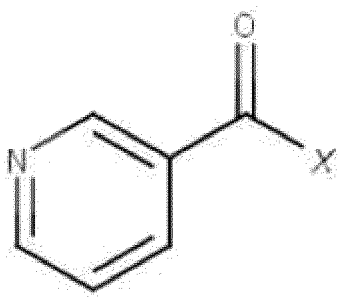
when said composition comprises at least one shogaol, then the mass ratio of [gingerol(s)/shogaol(s)] is greater than or equal to 1;

to induce and/or stimulate the growth of keratin fibers and/or impede their loss.

12. Non-therapeutic cosmetic use of a combination of active agents comprising:

- at least one compound having formula (I),

[Chem 1]



(I)

wherein

- *X* is the group OR or the group NRaRb
- Ra and Rb denote independently a hydrogen atom or a C1-C4 alkyl radical such as methyl, or Ra and Rb can form together with the nitrogen atom carrying them a 5- or 6-member heterocycle, said heterocycle being optionally substituted by one or more C1-C4 (hydroxy)alkyl radicals or one or more hydroxy radicals;
- R denotes a hydrogen atom or a C1-C4 alkyl radical such as ethyl or a C1-C4 (hydroxy)alkyl radical,

- at least one gingerol, and
- optionally at least one shogaol;

wherein the mass ratio of [compound(s) having formula (I)/gingerol(s)] is less than or equal to 150, and

when said composition comprises at least one shogaol, then the mass ratio of [gingerol(s)/shogaol(s)] is greater than or equal to 1;

to treat alopecia, in particular androgenetic alopecia.

13. Use according to any one of claims 11 to 12, wherein the keratin fibers are hair, eyelashes, body hairs, and/or eyebrows.

14. Non-therapeutic cosmetic use according to any one of claims 11 to 13, wherein said at least one gingerol is chosen from: [6]-gingerol, [8] gingerol and [10] gingerol.

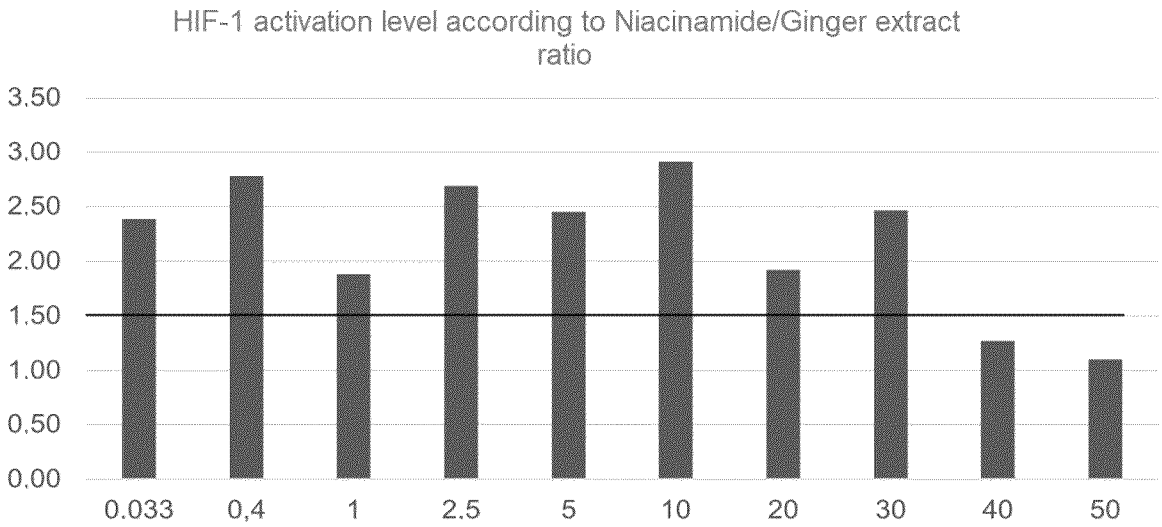

HIF-1 activation level according to Niacinamide/Ginger extract ratio
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
0.033
0,4
1
2.5
5
10
20
30
40
50

FIGURE. 1

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2024/087092

A. CLASSIFICATION OF SUBJECT MATTER

INV. A61K8/34 A61K8/67 A61K31/12 A61K31/455 A61P17/14
A61Q7/00 A61K8/49

ADD.

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 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 practicable, search terms used)

EPO-Internal, BIOSIS, CHEM ABS Data, EMBASE, SCISEARCH, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2008/049651 A1 (HENKEL KGAA [DE]; GODDINGER DIETER [DE]; DELOWSKY JENS [DE]) 2 May 2008 (2008-05-02)	1,5,7-13
Y	page 4, paragraph 3 page 9, last paragraph - page 10, paragraph 3 page 12, paragraph 1 page 106, paragraph 2 page 122; example 8a; table 16a page 122, paragraph 2 page 126; example 8a; table 18a page 126, paragraph 2 page 130; claim 8a; table 19a page 130, paragraph 2 claims 1, 9, 22, 23	6

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

[x] See patent family annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
18 March 2025	03/04/2025

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	Cielen, Elsie

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CN 116 725 925 A (ZHANGHUA COSMETICS TECH CO LTD) 12 September 2023 (2023-09-12)	1,5,7-13
Y	page 10, paragraph [0035] page 15, paragraph [0062] examples 1-1 examples 1-4comparatif claim 1	6

X	CN 111 110 618 B (WANDOU ZHIBEN (BEIJING) TECH CO LTD) 27 September 2022 (2022-09-27)	1,3-5, 7-13
Y	page 4, paragraph [0017]-[0018] examples 1-4 claims 1, 2, 4, 5	6

X	WO 2023/046730 A1 (BIONORICA SE [DE]) 30 March 2023 (2023-03-30) page 10, lines 14-26 page 34, line 33 - page 35, last line claims 1, 3, 4, 12-14	1-5

Y	EP 2 772 245 B1 (SYMRISE AG [DE]) 22 August 2018 (2018-08-22) page 2, paragraph [0001] page 3, paragraphs [0015], [0017]-[0018], [0021] pages 23-24, paragraph [0130] page 26; table 1 claim 1	1-14

Y	WATANABE Y ET AL: "Topical adenosine increases thick hair ratio in Japanese men with androgenetic alopecia", INTERNATIONAL JOURNAL OF COSMETIC SCIENCE, KLUWER ACADEMIC PUBLISHERS, DORDRECHT, NL, vol. 37, no. 6, 18 May 2015 (2015-05-18), pages 579-587, XP071470289, ISSN: 0142-5463, DOI: 10.1111/ICS.12235 abstract page 580, column 1, paragraph 1 page 582; figure 4 page 583; table II page 585, column 2, paragraph 1 page 585; table III	1-14

	-/--	

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	Utsa Ganguly: "Know How Niacinamide Is Beneficial For Hair", ABPLive, 11 June 2023 (2023-06-11), pages 1-4, XP093194864, Retrieved from the Internet: URL:https://news.abplive.com/lifestyle/how-niacinamide-is-beneficial-for-hair-sources-of-niacinamide-1605722 page 2, last paragraph - page 3, paragraph 1	1-14
X,P	WO 2024/126541 A1 (OREAL [FR]) 20 June 2024 (2024-06-20) page 24; table 1 claims 1, 3, 4, 12	1,3-13
Y	DATABASE GNPD [Online] MINTEL; 11 February 2020 (2020-02-11), anonymous: "Anti Hair-Fall Fortifying Treatment Ampoules", XP055950324, Database accession no. 7175899 abstract	6

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2024/087092

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2008049651 A1	02-05-2008	DE 102006050984 A1	30-04-2008
		WO 2008049651 A1	02-05-2008
CN 116725925 A	12-09-2023	NONE	
CN 111110618 B	27-09-2022	NONE	
WO 2023046730 A1	30-03-2023	EP 4405045 A1	31-07-2024
		WO 2023046730 A1	30-03-2023
EP 2772245 B1	22-08-2018	BR 102014004271 A2	06-10-2015
		CN 104000752 A	27-08-2014
		EP 2772245 A1	03-09-2014
		ES 2701758 T3	25-02-2019
		US 2014242020 A1	28-08-2014
WO 2024126541 A1	20-06-2024	FR 3143350 A1	21-06-2024
		WO 2024126541 A1	20-06-2024