Title: USE OF THE MMP-12 PROTEIN IN THE PREVENTION AND/OR TREATMENT OF DANDRUFF CONDITIONS OF THE SCALP

Abstract: The present invention relates to the cosmetic use of an effective amount of at least one active agent consisting of a polypeptide having at least 80% amino acid identity with a metalloproteinase MMP-12 of sequence chosen from SEQ ID NO: 1, SEQ ID NO: 2 and SEQ ID NO: 3, or a C-terminal fragment of said polypeptide, for preventing and/or treating dandruff conditions of the scalp, said polypeptide or said fragment comprising the sequence KDXK, in which X represents aspartic acid or glutamic acid.
USE OF THE MMP-12 PROTEIN IN THE PREVENTION AND/OR TREATMENT OF DANDRUFF CONDITIONS OF THE SCALP

The present invention is directed mainly towards proposing a novel active agent for preventing and/or treating dandruff conditions of the scalp.

The present invention relates to the use, in particular cosmetic use, of an effective amount of at least one active agent consisting of a polypeptide having at least 80% amino acid identity with the metalloproteinatease MMP-12 of sequence chosen from SEQ ID NO: 1, SEQ ID NO: 2 and SEQ ID NO: 3 indicated hereinafter, or a C-terminal fragment of this polypeptide, for preventing and/or treating dandruff conditions of the scalp. A polypeptide in accordance with the invention comprises the sequence KDXK, in which X represents aspartic acid or glutamic acid.

The skin is a tissue in which the cells are joined together and interlinked with one another. Skin tissue forms an external covering comprising sebaceous or sweat glands, and hair follicles. The skin, and in particular the scalp, are epithelia which undergo continual renewal. The renewal, or desquamation, is a coordinated and finely regulated process resulting in the insensible and invisible removal of superficial cells.

However, abnormal or irregular desquamation of the cells of the stratum corneum, for various reasons, can result in the formation of large, thick cell clusters which are visible to the naked eye and called "squames" or "dandruff" in the case of the scalp, or in other situations, in a thinning of the stratum corneum. Desquamation disorders, resulting from abnormal or irregular desquamation, can result in a fragility or even in a lack of the barrier properties of the epidermis.

By way of example of factors which promote the appearance of squames or dandruff, mention may be made of stress, the winter period, an excess of sebum, a hydration defect or colonization of the skin or the hair follicles by the yeast Malassezia sp. These factors especially have the common feature of causing and/or promoting skin inflammation. Such an inflammation reinforces the appearance or even increases the presence of squames or of dandruff. In particular, yeasts of Malassezia sp. type, which make up part of the normal commensal flora at the surface of the scalp in dandruff-free individuals, experience a substantial increase in their proportion in the case of dandruff, or in the case of associated seborrhoeic dermatitis. Imbalance of the scalp ecoflora is a factor that promotes or even reinforces the presence of dandruff.

The presence of squames or dandruff conditions can be recurring, frequent, chronic conditions which are socially debilitating owing to their obvious unsightly nature. What is more, dandruff conditions of the scalp or abnormal desquamation of the skin can be reflected by an impairment of the barrier function of the epidermis, or generate itching sensations or pruritus, resulting in scratching which amplifies the phenomenon of the appearance of squames or dandruff, and, in return, irritation of the scalp or the skin.
The dandruff conditions of the scalp may be of oily type or of dry type. Dry dandruff conditions of the scalp are more frequently manifested, and are amplified during skin hydration disorders, and especially during substantial dryness of the scalp epidermis. In addition, since the scalp is rich in sebaceous glands, a dandruff condition can develop more readily in the excessive presence of sebum and be more readily pruriginous. Thus, an excessive secretion of sebum, or hyperseborrhoea, promotes the appearance of an oily dandruff condition of the scalp, or oily dandruff, generally associated with displeasure, sensations of discomfort, aesthetic disorders, or even a pathological condition of the skin.

Dandruff conditions generally respond to various local or systemic treatments. However, the efficacy of these treatments is only suspensory and demands rigorous adherence on the part of the user (sufficient frequency of use and sufficient application time). However, daily and long-term use of these treatments can lead to a phenomenon of habituation, reducing their efficacy, the habituation generally being associated with a rebound phenomenon occurring when the treatment is stopped. This phenomenon manifests itself through hyperseborrhoea, which worsens the dandruff condition and impairs the barrier function of the scalp. Moreover, the aggressiveness of certain antidandruff active agents with respect to the epidermal cells or the scalp ecoflora may also affect the scalp's barrier functions and lead to worsening of the dandruff condition. Finally, the efficacy of antidandruff treatments is often slow to develop and requires rigorous application over the long term. This lag time often leads to failure to follow the treatment. Consequently, many failures arise in the use of these treatments.

There is thus still a need for novel active agents that are capable of exerting beneficial cosmetic or therapeutic action on dandruff conditions of the scalp.

There is also a need for active agents which make it possible to re-establish the scalp ecoflora and in particular to prevent excessive colonisation of the scalp by Malassezia sp.

There is also a need for novel compositions that are effective in preventing and/or treating oily or dry scalp conditions and that are pleasant and comfortable to use, thus promoting adherence to the treatment.

The object of the present invention is to satisfy these needs.

Thus, according to a first subject, the invention relates to the cosmetic use of an effective amount of at least one active agent consisting of a polypeptide having at least 80% amino acid identity with a metalloproteinase MMP-12 of sequence chosen from SEQ ID NO: 1, SEQ ID NO: 2 and SEQ ID NO: 3 indicated hereinafter, or a C-terminal fragment of this polypeptide, for preventing and/or treating dandruff conditions of the scalp, said polypeptide or said fragment comprising the sequence KDXK, in which X represents aspartic acid or glutamic acid.
According to another advantage, the use according to the invention may reduce and/or treat pruritus of the scalp subsequent to the presence of irritant metabolites resulting from sebum lipid metabolism by *Malassezia* sp.

According to another of its aspects, the present invention relates to a polypeptide having at least 80% amino acid identity with the metalloproteinase MMP-12 of sequence chosen from SEQ ID NO: 1, SEQ ID NO: 2 and SEQ ID NO: 3, or a C-terminal fragment of said polypeptide, for use thereof as an active agent in a pharmaceutical or dermatological composition intended for preventing and/or treating skin infections of the scalp caused by *Malassezia* sp., said polypeptide or said fragment comprising the sequence KDXK, in which X represents aspartic acid or glutamic acid.

According to another of its aspects, the present invention relates to a cosmetic and/or dermatological composition intended for preventing and/or treating dandruff conditions of the scalp, comprising, in a physiologically acceptable medium, at least one active agent in accordance with the invention, in combination with at least an effective amount of at least one additional agent chosen from antidandruff agents, antioxidants, and mixtures thereof, this additional agent being different from the active agent according to the invention.

According to the present invention, such a composition is used topically.

According to another of its aspects, the present invention relates to a process, especially a cosmetic process, for treating and/or preventing dandruff conditions of the scalp in an individual, comprising at least one step of topical administration to said individual of at least an effective amount of at least one active agent according to the invention, consisting of a polypeptide having at least 80% amino acid identity with the metalloproteinase MMP-12 of sequence chosen from SEQ ID NO: 1, SEQ ID NO: 2 and SEQ ID NO: 3, or a C-terminal fragment of said polypeptide, said polypeptide or said fragment comprising the sequence KDXK, in which X represents aspartic acid or glutamic acid.

A process of the invention is in particular advantageously implemented in individuals with a dandruff condition of the scalp.

The term "physiologically acceptable medium" is intended to mean a medium compatible with all keratin materials, such as the skin, the scalp, the nails, the mucous membranes, the eyes and the hair, or any other area of bodily skin, and in particular with the scalp. A physiologically acceptable medium is preferentially a cosmetically or dermatologically acceptable medium, i.e. a medium that has no unpleasant odour, colour or appearance, and that is entirely compatible with the route of administration under consideration, which in the present case is topical administration.

The term "preventing" or "prevention" is intended to mean, according to the invention, reducing the risk of recurrence or slowing down the occurrence of a given phenomenon for instance, according to one aspect of the present invention, the excessive colonisation of the scalp by *Malassezia* sp.
For the purpose of the invention, the term "effective amount" is intended to mean the minimum amount that is sufficient to observe the occurrence of a desired effect, namely, for example, the treatment of dandruff conditions of the scalp of an individual. Such an amount may be determined by any method known to those skilled in the art, for example by means of preliminary experimental tests.

**Active agent derived from the metalloproteinase MMP-12**

The present invention relates to the use of an effective amount of an active agent consisting of a polypeptide having at least 80% amino acid identity with the metalloproteinase MMP-12 of sequence SEQ ID NO: 1, SEQ ID NO: 2 and SEQ ID NO: 3 indicated hereinafter, or a C-terminal fragment of this polypeptide, as an active agent, said polypeptide or said fragment comprising the sequence KDXK, in which X represents aspartic acid or glutamic acid.

The matrix metalloproteinase MMP-12, or MMP-12, is a metalloproteinase belonging to the family of matrix metalloproteinases, which are enzymes that in particular have the role of degrading the extracellular matrix of connective tissues, and in particular of the skin. This family of enzymes plays an important role in a large number of essential physiological processes, such as morphogenesis, angiogenesis and tissue repair.

MMP-12, also known under the name macrophage lipase, is in particular known for its role in degrading elastin.

However, when they are expressed aberrantly or excessively, these enzymes may lead to the appearance of pathological conditions.

Thus, the role of MMP-12 in a certain number of pathological conditions such as arthritis, emphysema (Hautamaki *et al.* Macrophage elastase is required for cigarette smoke-induced emphysema in mice. Science 277, 2002-2004 (1997)) and vascular diseases (Curci *et al.* Expression and localization of macrophage elastase (matrix metalloproteinase-12) in abdominal aortic aneurysms. J. Clin. Invest. 102, 1900-1910 (1998)) has been demonstrated.

However, to the Applicant's knowledge, an activity of MMP-12 in connection with dandruff conditions of the scalp has never been described in the prior art.

For the purpose of the present invention, the "percentage identity" between two amino acid sequences is determined by comparing the two optimally aligned sequences by means of a comparison window.

The part of the amino acid sequence in the comparison window may thus comprise additions or deletions (for example "gaps") relative to the reference sequence (which does not comprise these additions or these deletions) so as to obtain an optimal alignment between the two sequences.
The percentage identity is calculated by determining the number of positions at which an identical amino acid is observed for the two compared sequences, followed by dividing the number of positions at which there is identity between the two amino acids by the total number of positions in the comparison window, and then multiplying the result by 100 in order to obtain the percentage amino acid identity between the two sequences.

The optimal alignment of the sequences for the comparison may be achieved by computer using known algorithms.

In an entirely preferred manner, the percentage sequence identity is determined using the CLUSTAL W software (version 1.82), the parameters being set as follows: (1) CPU MODE = ClustalW mp (2) ALIGNMENT = "full "; (3) OUTPUT FORMAT = " aln w/numbers " (4) OUTPUT ORDER = " aligned "; (5) COLOR ALIGNMENT = " no " (6) KTUP (word size) = " default "; (7) WINDOW LENGTH = " default "; (8) SCORE TYPE = " percent "; (9) TOPDIAG = " default "; (10) PAIRGAP = " default "; (11) PHYLOGENETIC TREE/TREE TYPE = " none "; (12) MATRIX = " default "; (13) GAP OPEN = " default "; (14) END GAPS = " default "; (15) GAP EXTENSION = " default "; (16) GAP DISTANCES = " default "; (17) TREE TYPE = " cladogram " and (18) TREE GRAP DISTANCES = " hide ".

A polypeptide or a C-terminal fragment thereof according to the invention may be synthesized via standard methods of synthetic chemistry, i.e. homogeneous chemical syntheses in solution or in solid phase. By way of illustration, those skilled in the art may use the polypeptide solution-synthesis techniques described by Houben Weil (1974, in Methode der Organischen Chemie, E. Wunsh ed., volume 15-1 and 15-11, Thieme, Stuttgart.). A polypeptide or a C-terminal fragment thereof according to the invention may also be synthesized chemically in liquid or solid phase by successive coupling of the various amino acid residues (from the N-terminal end to the C-terminal end in the liquid phase, or from the C-terminal end to the N-terminal end in the solid phase). Those skilled in the art may especially use the solid-phase peptide synthesis technique described by Merrifield (Merrifield R.B., (1965a), Nature, vol. 207 (996): 522-523; Merrifield R.B., (1965b), Science, vol. 150 (693): 178-185).

According to another aspect, a polypeptide or a C-terminal fragment thereof according to the invention may be synthesized by genetic recombination, for example according to a production process comprising the following steps:

(a) preparing an expression vector into which has been inserted a nucleic acid coding for the polypeptide or a C-terminal fragment thereof of the invention, said vector also comprising the regulatory sequences necessary for the expression of said nucleic acid in a chosen host cell;

(b) transfecting a host cell with the recombinant vector obtained in step (a);

(c) culturing the host cell transfected in step b) in a suitable culture medium;
(d) recovering the culture supernatant of the transfected cells or the cell lysate of said cells, for example by sonication or by osmotic shock; and

(e) separating or purifying, from said culture medium, or from the cell lysate pellet, the recombinant polypeptide or a recombinant C-terminal fragment thereof of the invention.

To purify a polypeptide or a C-terminal fragment thereof according to the invention that has been produced by host cells transfected or infected with a recombinant vector coding for said polypeptide or a C-terminal fragment thereof, those skilled in the art may advantageously use purification techniques described by Molinier-Frenkel (2002, J. Viral. 76, 127-135), by Karayan et al. (1994, Virology 782-795) or byNovelli et al. (1991, Virology 185, 365-376).

Preferably, the MMP-12 under consideration according to the invention is human and of sequence SEQ ID NO: 1 as defined in the present patent application.

According to one embodiment of the invention, a fragment of the C-terminal part of a polypeptide in accordance with the invention may also be used, on condition, however, that this fragment comprises the amino acid sequence KDXK.

K represents a lysine (abbreviated as Leu) and D represents an aspartic acid (abbreviated as Asp).

The amino acid defined as being X in the amino acid sequence KDXK mentioned previously is chosen from glutamic acid (abbreviated as Glu or E) and aspartic acid (abbreviated as Asp or D).

Such a C-terminal fragment that is suitable for use in the invention may comprise a sequence with a length of from 80 to 20 contiguous amino acids, or even from 50 to 20 contiguous amino acids and preferably from 30 to 20 contiguous amino acids of the C-terminal end the polypeptide.

According to one preferred embodiment, a C-terminal fragment of a polypeptide in accordance with the invention consists at least, continguously and in this order, of at least the 8 amino acids preceding the sequence KDXK according to the invention, the sequence KDXK itself, and then at least the 8 amino acids following the sequence KDXK in a polypeptide in accordance with the invention.

According to one preferred embodiment of the invention, the C-terminal fragment of a polypeptide in accordance with the invention, i.e. having at least 80% amino acid identity with the metalloproteinase MMP-12 of sequence chosen from SEQ ID NO: 1, SEQ ID NO: 2 and SEQ ID NO: 3 is chosen from the following sequences:

SEQ ID NO: 4: ARNQVFLFKDDKWLISNLR
SEQ ID NO: 5: GRNQLFLFKDEKYWLINNLV
SEQ ID NO: 6: SRNQLFLFKDEKYWLINNLV
According to one preferred embodiment, at least the amino acids constituting the sequence KDXK are in beta form.

According to one embodiment of the invention, an active agent in accordance with the invention consisting of a polypeptide having at least 80% amino acid identity with the metalloproteinase MMP-12 of sequence SEQ ID NO: 1, SEQ ID NO: 2 and SEQ ID NO: 3 indicated below, or a C-terminal fragment of this polypeptide, said polypeptide or said fragment comprising the sequence KDXK, in which X represents aspartic acid or glutamic acid, is used in a composition, especially a cosmetic composition, as defined below.

It may be present in such a composition in a content of between 0.0001% and 30% by weight, preferably between 0.001% and 15% by weight and preferentially between 0.1% and 10% by weight relative to the total weight of the composition.

**Composition**

The present invention relates to a cosmetic and/or dermatological composition intended for preventing and/or treating dandruff conditions of the scalp, comprising, in a physiologically acceptable medium, at least one active agent as defined previously.

Such a composition also comprises at least an effective amount of at least one agent chosen from antidandruff agents and antioxidants, other than the active agent defined previously, and mixtures thereof.

An additional antidandruff agent in accordance with the invention can be chosen from octopyrox, zinc pyrithione, salicylic acid, selenium disulfide, ketoconazole or other azole compounds, and mixtures thereof.

Such antidandruff agents may be present in a composition in accordance with the invention in a content of between 0.01% and 20% by weight, preferably between 0.1% and 10% by weight and preferentially between 0.1% and 5% by weight relative to the total weight of the composition.

An additional antioxidant in accordance with the invention may be chosen from tocopherol and esters thereof, in particular tocopheryl acetate; ascorbic acid and derivatives thereof, in particular magnesium ascorbyl phosphate and ascorbyl glucoside; ferulic acid; serine; ellagic acid, phloretin, polyphenols, tannins, tannic acid, epigallocatechins and natural extracts containing them, anthocyanins, rosemary extracts, olive leaf extracts, for instance those from the company Silab, green tea extracts, resveratrol and derivatives thereof, ergothioneine, N-acetylcysteine, an extract of the brown alga *Pelvetia canaliculata*, for instance Pelvetiane® from Secma, chlorogenic acid, biotin, chelating agents, such as BHT, BHA, N,N'-bis(3,4,5-trimethoxybenzyl)ethylenediamine and salts thereof; idebenone, plant extracts, for instance Pronalen Bioprotect TM from the company Provital;
coenzyme Q10, bioflavonoids, SODs, phytantriol, lignans, melatonin, pidolates, glutathione, caprylylglycol, phloretin, Totarol™ or extract of Podocarpus totara containing Totarol (totara-8,1 1,13-trienol or 2-phenanthrenol, 4b,5,6,7,8,8a,9,10-octahydro-4b,8,8-trimethyl-l-(l-methylethyl)-; a jasmine extract such as the product sold by Silab under the name Helisun®; hesperitin laurate such as Flavagrum PEG® from the company Engelhard Lyon; an extract of Paeonia suffruticosa root, such as the product sold by the company Ichimaru Pharcos under the name Botanpi Liquid B®; an extract of lychee such as the extract of lychee pericarp sold by the company Cognis under the name Litchiderm LS 9704®, and an extract of pomegranate fruit (Punica Granatum), such as the product sold by the company Draco Natural Products.

An antioxidant complex comprising vitamins C and E and at least one carotenoid, especially a carotenoid chosen from β-carotene, lycopene, astaxanthin, zeaxanthin and lutein, flavonoids such as catechins, extract of pomegranate, hesperidin, neohesperidin, proanthocyanidins and anthocyanins, may also be used. Such antioxidants may be present in a composition in accordance with the invention in a content of between 0.01% and 20% by weight, preferably between 0.05% and 10% by weight and preferentially between 0.05% and 5% by weight relative to the total weight of the composition.

Galenic formulation

The compositions in accordance with the invention are administered topically. They are therefore in the galenic forms suitable for this method of application.

They may in particular be aqueous, aqueous-alcoholic or oily solutions, solutions or dispersions of the lotion or serum type, emulsions of liquid or semi-liquid consistency of the milk type, obtained by dispersing a fatty phase in an aqueous phase (O/W) or conversely (W/O), or emulsions, of soft, semi-solid or solid consistency, of the cream type, aqueous or anhydrous gels, microemulsions, microcapsules, microparticles, or vesicular dispersions of ionic and/or nonionic type.

These compositions are prepared according to usual methods.

A composition intended for topical application according to the invention may advantageously be formulated in any galenic form that is suitable for haircare, especially in the form of a hair lotion, a shampoo, a hair conditioner, a disentangler, a hair cream or gel, a styling lacquer, a hairsetting lotion, a treating lotion, a dye composition (especially for oxidation dyeing) optionally in the form of a colouring shampoo, a hair-restructuring lotion, a permanent-waving composition, a lotion or gel for combating hair loss, an antiparasitic shampoo, a medicated shampoo, especially an antiseborrhoea shampoo, or a scalp care product, which is especially anti-irritant, anti-ageing or restructuring, or which activates the blood circulation.
According to one preferred embodiment, a composition according to the invention is in
the form of a cleansing cream, a mask, a lotion, a scalp treatment or care gel, a scalp care gel or
mousse, a cleansing or disinfecting lotion or a shampoo.

A composition of the invention may also comprise a fatty phase, said fatty phase being
preferentially between 5% and 80% by weight and preferably between 5% and 50% by weight relative
to the total weight of the composition, in particular when the composition according to the invention is
an emulsion.

The oils, emulsifiers and coemulsifiers used in the composition in emulsion form are
chosen from those conventionally used in cosmetics and/or dermatology.

The emulsifier and the coemulsifier may be present in a composition of the invention in a
proportion ranging from 0.3% to 30% by weight and preferably from 0.5% to 20% by weight relative
to the total weight of the composition.

When the composition of the invention is an oily solution or gel, the fatty phase may
represent more than 90% of the total weight of the composition.

In a known manner, the galenic forms intended for topical administration may also
contain adjuvants that are common in the cosmetic, pharmaceutical and/or dermatological field, such
as hydrophilic or lipophilic gelling agents, hydrophilic or lipophilic active agents, preserving agents,
antioxidants, solvents, fragrances, fillers, screening agents, odour absorbers and colorants.

The amounts of these various adjuvants are those conventionally used in the field under
consideration, for example from 0.01% to 20% of the total weight of the composition. Depending on
their nature, these adjuvants may be introduced into the fatty phase and/or into the aqueous phase.

As fatty substances that may be used in the invention, mention may be made of mineral
oils, for instance hydrogenated polyisobutene and liquid petroleum jelly, plant oils, for instance a
liquid fraction of shea butter, sunflower oil and apricot kernel oil, animal oils, for instance
perhydrosqualene, synthetic oils, especially purcellin oil, isopropyl myristate and ethylhexyl palmitate,
unsaturated fatty acids and fluoro oils, for instance perfluoropolyethers. It is also possible to use fatty
alcohols, fatty acids, for instance stearic acid and, for example, waxes, especially paraffin wax,
carnauba wax and beeswax. It is also possible to use silicone compounds, for instance silicone oils and
for example cyclomethicones and dimethicones, and silicone waxes, resins and gums.

As emulsifiers that may be used in the invention, mention may be made, for example, of
glyceryl stearate, polysorbate 60, the mixture of cetylstearyl alcohol/cetylstearyl alcohol
oxyethyleneated with 33 mol of ethylene oxide sold under the name Sinnowax AO® by the company
Henkel, the mixture of PEG-6/PEG-32/glycol stearate sold under the name Tefose® 63 by the
company Gattefosse, PPG-3 myristyl ether, silicone emulsifiers such as cetyl dimethicone copolyol,
and sorbitan monostearate or tristearate, PEG-40 stearate and oxyethyleneated (20 EO) sorbitan
monostearate.
As solvents that may be used in the invention, mention may be made of lower alcohols, in particular ethanol, isopropanol and propylene glycol.

According to one embodiment of the invention, a composition may comprise from 10% to 80% by weight of water, preferably from 20% to 70% by weight of water and preferentially from 30% to 60% of water relative to the total weight of the composition.

This water may advantageously be a spring and/or mineral water, chosen especially from Vittel water, waters from the Vichy basin and la Roche Posay water.

Hydrophilic gelling agents that may be mentioned include carboxylic polymers such as carbomer, acrylic copolymers such as acrylate/alkyl acrylate copolymers, polyacrylamides and especially the mixture of polyacrylamide, C_{13-14} isoparaffin and laureth-7 sold under the name Seigel 305® by the company SEPPIC, polysaccharides, for instance cellulose derivatives such as hydroxyalkylcelluloses and in particular hydroxypropylcellulose and hydroxyethylcellulose, natural gums such as guar gum, locust bean gum and xanthan gum, and clays.

Lipophilic gelling agents that may be mentioned include modified clays, for instance bentones, metal salts of fatty acids, for instance aluminium stearates and hydrophobic silica, or else ethylcellulose and polyethylene.

Additional agents:
A composition in accordance with the invention may also comprise at least one additional agent that is conventionally used, such as vitamins, and more particularly vitamins B3, B5, B6, B8, C, E, or PP, niacin, carotenoids, polyphenols and minerals such as zinc, calcium, magnesium, etc.

Antimicrobial agents different from a polypeptide having at least 80% amino acid identity with the metallopeptinase MMP-12 of sequence chosen from SEQ ID NO: 1, SEQ ID NO: 2 and SEQ ID NO: 3 indicated hereinafter, or a C-terminal fragment of this polypeptide, and comprising at least the sequence KDXK according to the invention, can also be used. Such antimicrobial agents can particularly be those mentioned in application DE 10324567 and can preferably be chosen from octopyrox, zinc pyrithione, salicylic acid, selenium disulfide, ketoconazole or other azole compounds, and mixtures thereof.

It may also be a case of at least one probiotic or a prebiotic, or a mixture of probiotics or of prebiotics. More particularly, these prebiotics may be chosen from oligosaccharides, produced from glucose, galactose, xylose, maltose, sucrose, lactose, starch, xylan, hemicellulose, inulin, gums of acacia type, for example, or a mixture thereof. More particularly, the oligosaccharide comprises at least one fructo-oligosaccharide. More particularly, this prebiotic may comprise a mixture of fructo-oligosaccharide and of inulin.

In the topical galenic forms according to the invention, it is more particularly possible to use as hydrophilic active agents proteins or protein hydrolysates, amino acids, other than a polypeptide
or a C-terminal fragment of this polypeptide in accordance with the invention, polyols, in particular C2 to C10 polyols, for instance glycerol, sorbitol, butylene glycol and polyethylene glycol, urea, allantoin, sugars and sugar derivatives, water-soluble vitamins, starch, and bacterial or plant extracts, for instance those from Aloe vera.

As regards the lipophilic active agents, retinol (vitamin A) and derivatives thereof, tocopherol (vitamin E) and derivatives thereof, ceramides, essential oils and unsaponifiable materials (tocotrienol, sesamine, gamma-oryzanol, phytosterols, squalenes, waxes and terpenes) may be used.

According to another embodiment of the invention, a composition according to the invention may comprise at least one anti-inflammatory.

Said anti-inflammatory may in particular be chosen from cortisone, hydrocortisone, indomethacin, betamethasone, azelaic acid, acetaminophen, diclofenac, clo betasol propionate, folic acid; an extract of Eperua falcata bark, such as the product sold by the company Cognis under the name Eperuline®; an extract of Paeonia suffruticosa root, such as the product sold by the company Ichimaru Pharmos under the name Botanpi Liquid B®; and mixtures thereof.

**Cosmetic treatment process**

As indicated previously, a process according to the invention may be performed by topical application, in particular by application to the scalp, of at least one active agent consisting of a polypeptide having at least 80% amino acid identity with the metalloproteinase MMP-12 of sequence chosen from SEQ ID NO: 1, SEQ ID NO: 2 and SEQ ID NO: 3, or a C-terminal fragment of said polypeptide as defined previously, for treating and/or preventing dandruff conditions of the scalp in an individual, said polypeptide or said fragment comprising the sequence KDXK, in which X represents aspartic acid or glutamic acid.

These dandruff conditions are in particular associated with a proliferation of pathogenic microorganisms on the scalp and/or and imbalance in the scalp ecoflora.

Advantageously, a process of the invention may comprise the topical application of a composition in accordance with the invention, in particular in the form of a cleansing cream, a lotion, a mask, a scalp treatment or care gel, a scalp care gel or mousse, a cleansing or disinfecting lotion or a shampoo.

A topical cosmetic process according to the invention may be performed, for example, on a daily basis, for instance at a rate of a single administration per day or one administration twice a day, for example once in the morning and once in the evening.

A topical cosmetic process according to the invention may be performed over a time period ranging from one week to several weeks, or even several months, this period moreover possibly being repeated after periods without treatment, for several months or even several years.
By way of example, the topical administration of a compound according to the invention may be repeated, for example, 2 to 3 times a day or more and generally over an extended period of at least 4 weeks, or even 4 to 15 weeks, with, where appropriate, one or more periods of interruption.

The present invention also discloses the use of an effective amount of at least one polypeptide having at least 80% amino acid identity with the metalloproteinase MMP-12 of sequence chosen from SEQ ID NO: 1, SEQ ID NO: 2 and SEQ ID NO: 3, or a C-terminal fragment of this polypeptide, for preparing a pharmaceutical or dermatological composition intended for preventing and/or treating skin infections of the scalp caused by *Malassezia* sp., said polypeptide or said fragment comprising the sequence KDXK, in which X represents aspartic acid or glutamic acid.

In the description and in the examples that follow, unless otherwise indicated, the percentages are percentages by weight and the ranges of values written in the form "between ... and ...") include the stated lower and upper limits.

The examples below are presented as non-limiting illustrations of the field of the invention.

**EXAMPLES**

1. **Topical compositions in accordance with the invention**

   **Example 1: scalp lotion**

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>% by weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polypeptide derived from MMP-12 (SEQ ID: 4)</td>
<td>5.00</td>
</tr>
<tr>
<td>Zinc pyrithione</td>
<td>2.00</td>
</tr>
<tr>
<td>Anti-inflammatory</td>
<td>0.05</td>
</tr>
<tr>
<td>Isopropanol</td>
<td>40.0</td>
</tr>
<tr>
<td>Preserving agent</td>
<td>0.30</td>
</tr>
<tr>
<td>Water</td>
<td>q.s 100</td>
</tr>
</tbody>
</table>
**Example 2: Scalp care milk**

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>% by weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polypeptide derived from MMP-12 (SEQ ID NO: 5)</td>
<td>5.00</td>
</tr>
<tr>
<td>Glyceryl stearate</td>
<td>1.00</td>
</tr>
<tr>
<td>Oil of cetylstearyl alcohol/cetylstearyl alcohol oxyethylenated with 30 mol OE (Sinnowax AO® sold by the company Henkel)</td>
<td>3.00</td>
</tr>
<tr>
<td>Cetyl alcohol</td>
<td>1.00</td>
</tr>
<tr>
<td>Dimethicone (DC 200 Fluid® sold by the company Dow Corning)</td>
<td>1.00</td>
</tr>
<tr>
<td>Liquid petroleum jelly</td>
<td>6.00</td>
</tr>
<tr>
<td>Isopropyl myristate (Estol® IMP 1514 sold by Unichema)</td>
<td>3.00</td>
</tr>
<tr>
<td>Antioxidant</td>
<td>0.05</td>
</tr>
<tr>
<td>Glycerol</td>
<td>20.00</td>
</tr>
<tr>
<td>Preserving agent</td>
<td>0.30</td>
</tr>
<tr>
<td>Water</td>
<td>q.s 100</td>
</tr>
</tbody>
</table>

2. **Clinical study of compositions in accordance with the invention**

In order to determine the antidandruff effect of a topical treatment, on the scalp, of a composition in accordance with the invention comprising a polypeptide derived from MMP-12 (SEQ ID NO: 4), a double-blind, randomized, controlled, comparative single-centre study was carried out on 2 groups of 33 individuals each.

One of these two groups used a composition in accordance with the invention, namely a composition in the form of a gel containing the polypeptide, water and carbopol, while the other group used only a "placebo" composition, identical to that used in the first group, except that it is free of active agent in accordance with the invention.

The individuals constituting these groups each applied to their scalp, daily for 61 days, the composition specific to the group to which they belonged.

After this period, a clinical evaluation of the dandruff condition of the scalp of each of these individuals was carried out by clinical scoring. The amount of free and adherent dandruff and of erythema and the seborrhoea of their scalp were thus evaluated, compared with the condition of their scalp before the 61-day period mentioned above.

In addition, the individuals themselves performed a self-evaluation of the dandruff condition, of the pruritus, of the oily condition, of the irritations, of the redness, of the tautness and of the overall perception of their scalp, compared with the condition in which it was before the application of the composition tested by each group.
The results obtained at the end of this clinical evaluation and of this self-evaluation show that the topical treatment of the scalp with a composition comprising an active agent in accordance with the invention leads, after 2 months of treatment, to a decrease in the dandruff conditions of the scalp.
Human metalloproteinase MMP-12 in its mature form (Homo sapiens)

SEP ID NO: 1
GPVWRKHYITYRNTPDMNREDVDYAI KAFQVWSNVTPLKFKINTGMA DILWFARAGAHGDFHAFDGKGGILAHAFGPGGSGIDGAHFDEDEFWTTHSSGTNLFLTAVHEI GSHLSGLGHSSDPKAVMFPTYKVDINTFRLSADDIRGQSLYGDPKENQRLPNPDPNLSDPAFDAVTT
VGNKIFFFFKDRFFWLKVSRPKTSVNLISSLWPTLPSGIEAAIEEARNQVFLFKDDKYWLISNLRPEP NYPKSIHSGFPNFVKKIDAAVFNPFRYRTYFFVDNQYWRYDERQMMDPGYPKLITKNFQGIGPKIDAVFYSK NKKYYFFQGSNQFEYEYDFLLQRTKTLKSNWSFGC

Mouse metalloproteinase MMP-12 (Mus musculus)

SEP ID NO: 2
RSRWMKRYLTYRINYTPDMKREDVDYIFpKAFpVWSVDVTPLFRKLIKEDADIMILFAFGAHGDFYFDGKGGTLAHAFYPGPpGDHAHFDEAEWTKSpGTNLFLVAHEGHLGSPHpHSNPKSIMYPTYRLNPSTFRLSADDINIpSLYGAPVKKPSLTpKPSSTFCpSLSFADVT
TVGKIFFFKDFWWKLPSPATNITSSSWPTPSIpAAYEIESRNPpLFLFKDEKYWLINNLVPPEPHYPSIYSLGFSASVKKVDAAVFDPLRpKVYFFVDKHYYRVDRpELMDPAYPKLIS
THFPGIRPKIDAVLYFKRHYYIpGAYpLEYDPLFRRVTKTLKTSWSFGC

Rat metalloproteinase MMP-12 in its mature form (Rattus norvegicus)

SEP ID NP: 3
RSRWMKRYLTYRINYTPDMKRADVDYIFpKAFpVWSVDVTPLRKRHIKGEADITILFAFGDHGDFYFDGKGGTLAHAFYPGPpGDHAHFDEAEWTKSfGTNLFLVAHEGHLGSPHHSNNP SIMYPTYRLPNTFRLSADDINIpSLYGAPVKKPSLTpKPSSTFCpSLSFADVT
TVGKIFFFKDFWWKLPSPATNITSSSWPTPSIpAAYEIGGRNpLFLFKDEKYWLINNLVPPEPHYPSIYSLGFSASVKKVDAAVFDPLRpKVYFFVDKHYYRVDRpELMDAAYPKLIS
THFPGIRPKIDAVLYFKRHYYIpGAYpLEYDPLFRRVTKTLKTSWSFGC

Peptide derived from Homo sapiens MMP-12

SEP ID NP: 4: ARNPVFLFKDDKYWLISNLR

Peptide derived from Mus musculus MMP-12

SEP ID NP: 5: GRNPFLFKDEKYWLINNLV

Peptide derived from Rattus norvegicus MMP-12

SEP ID NP: 6: SRNPFLFKDEKYWLINNLV
CLAIMS

1. Cosmetic use of an effective amount of at least one active agent consisting of a polypeptide having at least 80% amino acid identity with a metalloproteinase MMP-12 of sequence chosen from SEQ ID NO: 1, SEQ ID NO: 2 and SEQ ID NO: 3, or a C-terminal fragment of said polypeptide, for preventing and/or treating dandruff conditions of the scalp, said polypeptide or said fragment comprising the sequence KDXK, in which X represents aspartic acid or glutamic acid.

2. Use according to Claim 1, characterized in that the active agent used is a C-terminal fraction of said polypeptide, with a length of from 80 to 20 amino acids, preferably from 50 to 20 amino acids and preferentially from 30 to 20 amino acids and comprising the sequence KDXK, in which X represents aspartic acid or glutamic acid.

3. Use according to either one of Claims 1 and 2, characterized in that the active agent used according to the present invention is chosen from the sequences SEQ ID NO: 4, SEQ ID NO: 5, and SEQ ID NO: 6.

4. Polypeptide having at least 80% amino acid identity with the metalloproteinase MMP-12 of sequence chosen from SEQ ID NO: 1, SEQ ID NO: 2 and SEQ ID NO: 3, or a C-terminal fragment of said polypeptide, for use thereof as an active agent in a pharmaceutical or dermatological composition intended for preventing and/or treating skin infections of the scalp caused by Malassezia sp., said polypeptide or said fragment comprising the sequence KDXK, in which X represents aspartic acid or glutamic acid.

5. Cosmetic and/or dermatological composition intended for preventing and/or treating dandruff conditions of the scalp, comprising, in a physiologically acceptable medium, at least one active agent as defined in any one of Claims 1 to 3, in combination with at least an effective amount of at least one additional agent chosen from antidandruff agents, antioxidants, and mixtures thereof, this additional agent being different from the active agent defined according to any one of Claims 1 to 3.

6. Composition according to the preceding claim, characterized in that the active agent as defined in Claims 1 to 3 is used in a content of between 0.0001% and 30% by weight, preferably between 0.00% and 15% by weight and preferentially between 0.1% and 10% by weight relative to the total weight of the composition.

7. Composition according to either one of Claims 5 and 6, characterized in that said additional agent is present in a content of between 0.01% and 20% by weight, preferably between 0.1% and 10% by weight and preferentially between 0.1% and 5% by weight relative to the total weight of the composition.

8. Composition according to any one of Claims 5 to 7, characterized in that said composition also comprises at least one fatty phase, preferably in a content of between 5% and 80%
by weight and preferentially between 5% and 50% by weight relative to the total weight of the composition.

9. Composition according to any one of Claims 5 to 8, characterized in that it comprises from 10% to 80% by weight of water, preferably from 20% to 70% by weight of water and preferentially from 30% to 60% by weight of water relative to the total weight of the composition.

10. Composition according to any one of Claims 5 to 9, characterized in that it is in the form of a cleansing cream, a lotion, a mask, a scalp treatment or care gel, a scalp care gel or mousse, a cleansing or disinfecting lotion or a shampoo.

11. Cosmetic process for treating and/or preventing dandruff conditions of the scalp in an individual, comprising at least one step of topical administration to said individual of at least an effective amount of at least one active agent as defined in any one of Claims 1 to 3.

12. Process according to Claim 11, characterized in that said effective amount of at least one active agent as defined in any one of Claims 1 to 3 is used in a composition as defined in any one of Claims 5 to 10.

13. Process according to either one of Claims 11 or 12, characterized in that said step of administration to an individual is carried out by application to the scalp of an active agent as defined in any one of Claims 1 to 3, or of the composition as defined in any one of Claims 5 to 10.