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(54) **Title**: COMBINATION OF REDUCED GLUTATHIONE AND AMINO ACIDS FOR IMPROVING THE QUALITY OF THE HAIR IN WOMEN

(57) **Abstract**: The invention relates to the cosmetic use, by the oral and/or topical route, of combinations of reduced glutathione or one of its antioxidant analogues or precursors and two or more amino acids chosen from glutamic acid, threonine, glutamine, leucine, asparagine and tyrosine for improving the quality and/or preventing and/or treating a detrimental change in the quality of the hair in women.

Combination of reduced glutathione and amino acids for improving the quality of the hair in women

The present invention relates to the field of hair care. More particularly, it is targeted at providing combinations of use in improving the quality of the hair and/or hair fibres in women, in particular combating ageing of keratinous fibres and more particularly hair fibres, and most generally in protecting the hair in women, or combating hair loss and/or alopecia in women.

The individual hairs are produced in hair follicles formed of epithelial sheaths of epidermal origin and of a hair bulb comprising bulbar keratinocytes in a permanent state of division during the phases of growth of the individual hair. The individual hair is composed mainly of 85-90% proteins.

It is regarded as desirable by most women to have healthy and strong hair throughout life.

A great many cosmetic compositions comprising amino acids, in particular glutamine, arginine and cysteine, or peptides and/or taurine exist for the care of the scalp.

By way of example, the document EP 1 515 712 describes the use of taurine and/or hypotaurine and/or their salts acceptable in an oral composition for the preparation of an oral composition of use in the treatment and prevention of ageing of the pilosebaceous unit and/or of alopecia.

In addition, the document WO 99/62462 describes a composition for topical application on the hair for the treatment or prevention of its detrimental change comprising (i) cholesterol and (ii) an agent beneficial for the hair based on a mixture of an amino acid and a fatty acid, more particularly L-arginine and oleic acid.

The document WO 2007/068400 describes, for its part, a composition for the hair which comprises a mixture of sugar, an aliphatic amino acid and a basic amino acid. These compositions are more particularly intended for the treatment of hair which is dry, is damaged and/or demonstrates difficulties in manageability.

On the other hand, there does not currently exist compositions specifically suited to the prevention of the detrimental change in the quality of the hair which appears in particular with age in women, more particularly due to a specific deficiency of the hair follicle in amino acids, peptides or peptide derivatives.

Besides, to date, no composition exists that is specifically suited to the

treatment and/or prevention of the loss of hair fibres and more particularly of the hair and/or of alopecia in women, more particularly caused by a specific deficiency, of the hair follicle, in amino acids, peptides or peptide derivatives.

The specific deficiency pf the hair follicle, in amino acids, peptides or peptide derivatives is advantageously determined by reporting the amount in hair follicles of each amino acid relative to the total amount of amino acids, peptides and peptide derivatives.

The present invention is targeted specifically at meeting these needs by providing combinations of reduced glutathione or one of its antioxidant analogues or precursors and two or more amino acids chosen from glutamic acid, threonine, glutamine, leucine, asparagine and tyrosine.

The main subject matter of the invention is thus the cosmetic use by the oral and/or topical route, of a combination of reduced glutathione or one of its antioxidant analogues or precursors and two or more amino acids chosen from glutamic acid, threonine, glutamine, leucine, asparagine and tyrosine for improving the quality and/or preventing and/or treating a detrimental change in the quality of the hair in women.

FIRST EMBODIMENT

According to one first embodiment, the present invention is targeted specifically at preventing the detrimental change in the quality of the hair which appears in particular with age in women, more particularly due to a specific deficiency of the hair follicle in amino acids, peptides or peptide derivatives by providing a combination of glutamic acid, reduced glutathione or one of its antioxidant analogues or precursors and threonine.

This is because the inventors have found that such a combination of glutamic acid, reduced glutathione or one of its antioxidant analogues or precursors and threonine proves to be very particularly effective in haircare and for remedying a detrimental change in the quality of the hair which appears in particular with age, as is illustrated in particular in Example 1 below.

According to this first embodiment of the invention, the main subject-matter is thus the cosmetic use, by the oral and/or topical route, of a combination of glutamic acid, reduced glutathione or one of its antioxidant analogues or precursors and threonine for preventing and/or treating weak, brittle, lifeless or thinned hair, preventing and/or treating

split ends, improving the softness and the strength of the fibre or improving the volume of the hair and its sheen in women.

Another subject-matter according to the first embodiment of the invention is a cosmetic and/or pharmaceutical composition comprising, as sole amino acids, glutamic acid and threonine in combination with reduced glutathione or one of its antioxidant analogues or precursors.

A further subject-matter of the first embodiment of the invention is the cosmetic use of a combination or composition in accordance with the first embodiment of the present invention for preventing and/or treating weak, brittle, lifeless or thinned hair, preventing and/or treating split ends, improving the softness felt by the consumer, improving the strength of the fibre and improving the volume of the hair and its sheen in women.

The invention also relates according to its first embodiment, to a method for the cosmetic treatment of the hair in women which is intended to improve the quality of the hair and/or hair fibres, characterized in that it comprises at least the administration by the oral route or the topical application of a combination or composition in accordance with the first embodiment of the invention optionally comprising, in addition, supplementary amino acids, peptides or peptide derivatives as defined below.

In particular, the cosmetic use and/or the cosmetic treatment method according to the first embodiment of the invention makes it possible to protect aged hair.

In particular, the cosmetic use and/or the cosmetic treatment method according to the first embodiment of the invention makes it possible to prevent and/or limit the formation of thin and/or lifeless and/or brittle and/or weak hair.

The cosmetic use and/or the cosmetic treatment method according to the first embodiment of the invention also makes it possible to improve the quality of the keratinous fibres, in particular by promoting the growth of shiny and/or thick and/or strong hair.

Finally, the invention according to the first embodiment relates to a food supplement or a functional food comprising a portion of the compounds forming the combination of active principles in accordance with the first embodiment of the invention in a first composition and at least the other portion of the compounds of the combination in accordance with the first embodiment of the invention in a second composition, as kit or

combination product for a use which is simultaneous, separated or spread out over time.

Chronological ageing is a natural phenomenon which becomes apparent gradually and sooner or later depending on the individual. The outward signs of ageing on the hair can, however, be accelerated by endogenous factors, such as stress, illnesses, and the like, or exogenous factors, such as pollution, exposure to UV radiation, and the like.

The detrimental changes in the quality of the hair which appear in particular with age consist in particular of a change in appearance of the fibre: individual hair which is thin, lifeless, without strength (weak), lacklustre, greying.

The first embodiment of the invention results in particular from the observation by the inventors of a significant modification in the aminogram or the hair profile of amino acids, peptides or peptide derivatives of the hair follicle of an elderly woman *vs.* a young woman. As emerges from the example 1 presented below, some amino acids prove to be advantageous markers in detecting or diagnosing the risk of outward signs of a detrimental change in the quality of the hair in women.

According to a specific variant, the combination of active principles in accordance with the first embodiment of the present invention represents the only active substance of the composition according to the first embodiment of the invention.

According to one variant of this first embodiment of the invention, glutathione, glutamic acid and threonine are employed in amounts such that the amount of glutamic acid is greater than the amount of glutathione and this amount is itself greater than the amount of threonine.

According to a specific variant of this first embodiment of the invention, the ratio by weight of reduced glutathione to glutamic acid is between 0.1 and 1.5, in particular between 0.5 and 1 and more particularly between 0.6 and 0.9.

According to another specific variant of this first embodiment of the invention, the ratio by weight of threonine to glutamic acid is between 0.07 and 0.4, in particular between 0.1 and 0.3 and more particularly between 0.15 and 0.25.

According to one variant of the first embodiment of the invention, the combination can be employed with, in addition, at least one of the amino acids chosen from the group constituting of taurine, glutamine, glycine and optionally aspartic acid,

serine and alanine.

In the context of the present invention, all of the abovementioned optional amino acids are called supplementary amino acids, peptides or peptide derivatives. These supplementary amino acids, peptides or peptide derivatives are listed above by order of preference according to said first embodiment of the invention.

According to an alternative form of this variant, the composition employed comprises the combination of the amino acids glutamic acid reduced glutathione or one of its antioxidant analogues or precursors and threonine, and also all of the abovementioned supplementary amino acids.

Still according to this alternative form, the ratios by weight of the amino acids, peptides or peptide derivatives, whether main or supplementary, can be related to the content of taurine, which is the predominant peptide derivative in the hair profile of amino acids, peptides or peptide derivatives.

The ratios by weight reported below should be understood as being able to be considered separately or simultaneously.

Thus, according to this alternative form, the ratios by weight of glutamine and glycine, taken independently, to taurine are between 0.2 and 0.6, in particular between 0.3 and 0.5; the ratios by weight of aspartic acid, serine and alanine, taken independently, to taurine are between 0.1 and 0.5, preferably between 0.2 and 0.4.

As regards the reinforced ratios by weight of the active principles of the combination according to the first embodiment of the invention, the ratio by weight of glutamic acid to taurine is greater than 0.6; the ratio by weight of reduced glutathione or one of its antioxidant analogues or precursors to taurine is greater than 0.4; and/or the ratio by weight of threonine to taurine is greater than 0.1.

Still according to this alternative form, a composition according to the first embodiment of the present invention can comprise from 1 to 5% by weight of taurine, with respect to the total weight of the composition.

According to a specific variant, the invention according to its first embodiment relates to a composition in accordance with the first embodiment of the present invention, characterized in that it additionally comprises taurine, glutamine, glycine and optionally aspartic acid, serine and alanine and in that the ratios by weight of glutamine and glycine, taken independently, to taurine are between 0.2 and 0.6, in particular between 0.3 and 0.5;

the ratios by weight of aspartic acid, serine and alanine, taken independently, to taurine are between 0.1 and 0.5, preferably between 0.2 and 0.4; the ratio by weight of glutamic acid to taurine is greater than 0.6; the ratio by weight of reduced glutathione or one of its antioxidant analogues or precursors to taurine is greater than 0.4; and/or the ratio by weight of threonine to taurine is greater than 0.1.

Taurine is an amino acid derivative also known under the name of 2-amino-ethanesulphonic acid.

The combination of active principles in accordance with this first embodiment of the present invention can in particular be administered by the oral route in a proportion of a content of glutamic acid of 30 to 300 mg/day, in particular of 50 to 200 mg/day, more particularly still of 80 to 180 mg/day and in particular between 120 and 170 mg/day.

The compositions intended for administration by the oral route can in particular comprise all or a portion only of the daily dose. In other words, one to three compositions can be administered daily.

For example, an oral composition according to this first embodiment of the present invention can comprise from 10 to 300 mg of glutamic acid, in particular from 20 to 200 mg, especially from 30 to 170 mg.

Still by way of example, in the case where two daily compositions according to the first embodiment of the invention are administered, the oral composition can comprise from 15 to 150 mg of glutamic acid, in particular from 25 to 100 mg, especially from 40 to 60 mg.

Thus, another subject-matter of this first embodiment of the present invention is a method for the cosmetic treatment of the hair in women which is intended to improve the quality of the hair and/or hair fibres in women, characterized in that it comprises at least the administration by the oral route of a combination in accordance with the second embodiment of the invention, in particular in the form of a food supplement or functional food.

This treatment method according to this first embodiment of the invention exhibits the characteristics of a cosmetic method insofar as it makes it possible to improve the attractiveness of the hair, in particular by combating the detrimental change in the quality of the hair which appears especially with age. In addition, it can be used daily for

several months without a medical prescription.

In the case of the topical route, the content of glutamic acid can be between 2 and 12% by weight, in particular between 5 and 10% by weight and more particularly still between 6 and 8% by weight, with respect to the total weight of the composition comprising the combination in accordance with said first embodiment of the invention.

Thus, another subject-matter of the first embodiment of the present invention is a method for the cosmetic treatment of the hair in women which is intended to improve the quality of the hair and/or hair fibres in women, characterized in that it comprises at least the application, to the hair, of a cosmetic composition comprising an effective amount of at least one combination of active principles in accordance with the first embodiment of the present invention, in leaving the latter in contact with the hair and optionally rinsing the hair.

More specifically, a subject-matter of the first embodiment of the present invention is a method for the cosmetic care of the hair in women for the purpose of improving its condition and/or its appearance, in particular by combating the detrimental change in the quality of the hair which appears especially with age, characterized in that it consists in applying, to the hair and/or scalp, a cosmetic composition comprising at least one combination of active principles in accordance with the first embodiment of the present invention, in leaving the latter in contact with the hair and/or scalp and optionally in rinsing the hair and/or scalp.

Advantageously, in the method according to the first embodiment of the invention, between 5 µl and 1 ml of a solution or composition as defined above, comprising from 2 to 12% by weight of glutamic acid, in particular from 5 to 10% by weight and more particularly still between 6 and 8% by weight, with respect to the total weight of the composition of the first embodiment of the invention, are applied to the scalp. In order to improve the effectiveness of the method, the scalp can advantageously be massaged, manually or using an instrument.

SECOND EMBODIMENT

According to a second embodiment of the invention, the present invention aims precisely to treat and/or prevent the loss of hair fibres and more particularly of the hair

and/or of alopecia in women, more particularly caused by a specific deficiency, of the hair follicle, in amino acids, peptides or peptide derivatives by proposing a combination of reduced glutathione, or an antioxidant precursor or analogue thereof, of glutamine, of leucine, of asparagine and of tyrosine.

The inventors have in fact noted that such a combination of reduced glutathione, or an antioxidant precursor or analogue thereof, of glutamine, of leucine, of asparagine and of tyrosine is found to be most particularly effective for hair care and for remedying an alopecic condition and/or a condition favourable to accelerated and/or abundant hair loss, as is in particular illustrated in Example 2 hereinafter.

According to this second embodiment of the invention, the main subject is therefore the oral and/or topical cosmetic use of a combination of reduced glutathione, or an antioxidant precursor or analogue thereof, of glutamine, of leucine, of asparagine and of tyrosine, for preventing and/or treating hair loss and/or alopecia in women.

A subject according to this second embodiment of the invention is also the use of a combination of reduced glutathione, or an antioxidant precursor or analogue thereof, of glutamine, of leucine, of asparagine and of tyrosine, for the preparation of a pharmaceutical composition for use in treating alopecia in women.

Another subject-matter according to the second embodiment of the invention is a cosmetic and/or pharmaceutical composition comprising, as sole amino acids, glutamine, leucine, asparagine and tyrosine in combination with reduced glutathione or an antioxidant precursor or analogue thereof.

A further subject-matter of the second embodiment of the invention is the cosmetic use of a composition in accordance with the present invention for preventing and/or treating hair loss and/or alopecia in women.

The invention also relates according to its second embodiment to a method for cosmetic treatment of the hair in women, including of the scalp, intended to stimulate hair growth in women and/or prevent and/or reduce hair loss, characterized in that it comprises at least the oral administration or the topical application of a combination or composition in accordance with the second embodiment of the invention, with optionally, in addition, one or more supplementary amino acids, peptides or peptide derivatives as defined hereinafter.

Finally, according to its second embodiment, the invention relates to a food

supplement or a functional food comprising a part of the compounds forming the combination of active agents in accordance with the second embodiment of the invention in a first composition and at least the other part of the compounds of the combination in accordance with the second embodiment of the invention in a second composition, as a kit or combination product for simultaneous, separate or sequential use.

Alopecia is more particularly reflected by partial or total hair loss in an individual. Individuals in whom an alopecic condition manifests itself may, in particular, be the victim of diffuse alopecia such as, for example, androgenetic alopecia or seborrhoeic alopecia or alternatively common baldness due to an excess of androgens (male hormones). This type of alopecia is hereditary and therefore progressive, irreversible and responsible for most baldness. In a large number of cases, premature hair loss occurs in individuals who are genetically predisposed; this is then androchronogenetic alopecia ; this form of alopecia may involve women.

The second embodiment of the invention results in particular from the observation, by the inventors, of a significant modification of the aminogram or alternatively the hair amino acid, peptide or peptide derivative profile of the hair follicle of a woman subject to a phenomenon of alopecia, versus a woman of the same age without this manifestation. As emerges from the example 2 presented hereinafter, certain amino acids are found to be important markers for detecting or diagnosing the risk of manifestation of alopecia in women.

According to a specific variant, the combination of active principles in accordance with the second embodiment of the present invention represents the only active substance of the composition according to the second embodiment of the invention.

According to one particular variant of the second embodiment of the invention, the reduced glutathione or an antioxidant precursor or analogue thereof, the glutamine, the leucine, the asparagine and the tyrosine are used in respective amounts such that the amounts of reduced glutathione or an antioxidant precursor or analogue thereof and glutamine are equivalent and greater than the amount of leucine, the latter being greater than the amount of asparagine, which is itself equal to the amount of tyrosine.

According to one particular variant of this second embodiment of the invention, the ratio by mass between glutamine and reduced glutathione is between 0.5 and

1.5, in particular between 0.7 and 1.3, and more particularly between 0.9 and 1.1.

According to another particular variant of this second embodiment of the invention, the ratio by mass between leucine and reduced glutathione is between 0.07 and 0.7, in particular between 0.1 and 0.5, and more particularly between 0.2 and 0.4.

According to yet another particular variant of this second embodiment of the invention, the ratio by mass between asparagine and tyrosine, taken independently, and reduced glutathione is between 0.05 and 0.3, in particular between 0.07 and 0.2 and more particularly between 0.09 and 0.15.

According to one variant of this second embodiment of the invention, the combination may be used with, in addition, at least one of the amino acids, peptides or peptide derivatives chosen from the group consituted of taurine, glutamic acid, glycine, aspartic acid, serine and alanine. These amino acids, peptides or peptide derivatives are referred to as supplementary amino acids, peptides or peptide derivatives in the context of the present invention. These supplementary amino acids, peptides or peptide derivatives are listed above in order of preference according to said second embodiment of the invention.

According to an alternative form of this variant, a composition comprising the combination of the amino acids reduced glutathione, or an antioxidant precursor or analogue thereof, glutamine, leucine, asparagine and tyrosine, and also all the supplementary amino acids mentioned above, is used.

Still according to this alternative form, the ratios by mass between the amino acids, peptides or peptide derivatives, whether they are principal or supplementary, may be related to the content of taurine, which is the predominant peptide derivative in the hair amino acid, peptide or peptide derivative profile.

It should be understood that the ratios by mass reported hereinafter can be considered separately or simultaneously.

Thus, according to this alternative form, the ratio by mass between glutamic acid and taurine is between 0.4 and 0.8, preferably between 0.5 and 0.7; the ratio by mass between glycine and taurine is between 0.2 and 0.6, preferably between 0.3 and 0.5; and the ratios by mass between aspartic acid, serine and alanine, taken independently, and taurine are between 0.1 and 0.5, preferably between 0.2 and 0.4.

As regards the reinforced ratios by mass of the active agents of the combination in accordance with the second embodiment of the invention, the ratios by mass between glutamine and reduced glutathione, taken independently, and taurine is greater than 0.4; the ratio by mass between leucine and taurine is greater than 0.3 and/or the ratio by mass between asparagine and tyrosine is greater than 0.1.

Still according to this alternative form, a composition according to the second embodiment of the present invention may comprise from 1% to 5% by weight of taurine, relative to the total weight of the composition.

According to a specific variant, the invention according to its second embodiment relates to a composition in accordance with the second embodiment of the present invention, characterized in that it also contains taurine, glutamic acid, glycine, and optionally aspartic acid, serine and alanine, and in that the ratio by mass between glutamic acid and taurine is between 0.4 and 0.8, preferably between 0.5 and 0.7; the ratio by mass between glycine and taurine is between 0.2 and 0.6, preferably between 0.3 and 0.5; the ratios by mass between aspartic acid, serine and alanine, taken independently, and taurine are between 0.1 and 0.5, preferably between 0.2 and 0.4; the ratios by mass between glutamine and reduced glutathione, taken independently, and taurine are greater than 0.4; the ratio by mass between leucine and taurine is greater than 0.3 and/or the ratio by mass between asparagine and tyrosine is greater than 0.1.

The combination of active agents in accordance with this second embodiment of the present invention may in particular be administered orally, at a content of from 30 to 300 mg/day, in particular from 50 to 200 mg/day, even more particularly from 80 to 180 mg/day, and especially between 120 and 170 mg/day with respect to reduced glutathione or reduced glutathione equivalent.

The compositions for oral administration may in particular comprise all or only a part of the daily dose. In other words, one to three compositions may be administered per day.

For example, an oral composition according to this second embodiment of the present invention may contain from 10 to 300 mg of reduced glutathione or reduced glutathione equivalent, especially from 20 to 200 mg, in particular from 30 to 170 mg.

Still by way of example, when two daily compositions according to this second

embodiment of the invention are administered, the oral composition may contain from 15 to 150 mg of reduced glutathione or reduced glutathione equivalent, especially from 25 to 100 mg, in particular from 40 to 60 mg.

Thus, another subject-matter of this second embodiment of the present invention is also a method for cosmetic treatment of the hair, including the scalp, in women, intended to stimulate hair growth in women and/or prevent and/or reduce hair loss, characterized in that it comprises at least the oral administration of a combination in accordance with the second embodiment of the invention or of a composition containing same, in particular in the form of a food supplement or of a functional food, comprising an effective amount of at least one combination of active agents in accordance with the second embodiment of the present invention, in particular in the contents specified above.

This treatment method according to this second embodiment of the invention exhibits the characteristics of a cosmetic method insofar as it makes it possible to improve the aesthetics of the head of hair, avoiding hair loss. In addition, it can be used daily for several months, without medical prescription.

In the case of topical application, the content with respect to reduced glutathione, or reduced glutathione equivalent, may be between 2% and 12% by weight of the composition according to the second embodiment of the invention, in particular between 5% and 10% by weight, and even more particularly between 6% and 8% by weight, relative to the total weight of the composition, as reduced glutathione mass equivalent.

Thus, another subject-matter of the second embodiment of the present invention is also a method for cosmetic treatment of the hair, including the scalp, in women, intended to stimulate hair growth in women and/or reduce hair loss, characterized in that it comprises at least applying, to the hair, a cosmetic composition comprising an effective amount of at least one combination of active agents in accordance with the second embodiment of the present invention, leaving said composition in contact with the hair and, optionally, rinsing the hair.

More especially, a subject of the second embodiment of the present invention is a method for cosmetic care of the hair and/or of the scalp in women, with a view to improving the condition and/or the appearance of said hair and/or scalp, characterized in

that it consists in applying, to the hair and/or the scalp, a cosmetic composition comprising at least one combination of active agents in accordance with the second embodiment of the present invention, in leaving said composition in contact with the hair and/or the scalp and, optionally, in rinsing the hair and/or the scalp.

Advantageously, in the method according to the second embodiment of the invention, between 5 μl and 1 ml of a solution or composition as defined above, comprising from 2% to 12% by weight with respect to reduced glutathione, or reduced glutathione equivalent, in particular from 5% to 10% by weight, and even more particularly between 6% and 8% by weight, relative to the total weight of the composition of the second embodiment of the invention, are applied to the areas of the scalp that are to be treated. In order to improve the effectiveness of the method, the scalp may advantageously be massaged manually or using an instrument.

It is understood, in the context of the present invention, that "the cosmetic use by the oral and/or topical route" covers the use of products administered by the oral and/or topical route, these products being, for example, in the form of a food supplement or functional food, as set out below for the case of the oral route, producing an effect, on the hair, including the scalp, at the attractiveness or comfort level, or also for beauty purposes, for example with a view to protecting it, to keeping it in good condition, to modifying the appearance thereof and in particular to making it more attractive.

Likewise, within the meaning of the present invention, a "cosmetic composition" denotes a composition capable of producing an effect on the hair at the attractiveness and comfort level, or also for beauty purposes, namely, in the context of the first embodiment of the present invention, to keep it in good condition, more particularly to prevent and/or combat the detrimental change in the quality of the hair but also to improve the quality of the hair and/or hair fibres, and in the context of the second embodiment of the present invention, to combat and/or prevent hair loss. It can be provided in the form of a nutritional product.

The compositions in accordance with the present invention can also be intended for the treatment of domestic animals, in particular pets, such as dogs and cats. Thus, the compositions in accordance with the first embodiment of the invention may be of

use in the treatment and/or prevention of a detrimental change in the quality of the coats which appear in particular with age and can also be administered orally or applied topically.

On the other hand, the compositions according to the second embodiment of the invention may be of use in the treatment and/or prevention of body-hair loss and may also be administered orally or applied topically.

Glutamic acid, threonine, glutamine, leucine, asparagine and tyrosine are free natural amino acids.

While remaining within the context of the present invention, some nonessential amino acids may be replaced with essential amino acids. Thus, the tyrosine present in the combination of active agents in accordance with the second embodiment of the present invention may be replaced with phenylalanine.

Glutathione is a tripeptide of glutamic acid, cysteine and glycine. Glutathione can exist, via the thiol functional group of the cysteine radical, in a reduced form; the term used is reduced glutathione.

Glutathione can be replaced by its analogues or precursors. Thus, reduced glutathione can be replaced by its antioxidant analogues or precursors.

In such a case, the contents by weight are calculated as reduced glutathione equivalent.The amino acids can be provided in their D or L form, preferably in the L form.

The constituent amino acids of the active principles can be provided in the form of a protein hydrolysate or of a combination of several protein hydrolysates or also can be obtained by biotechnology processes.

According to a specific variant, the constituent amino acids of the active principles are provided in the form of a protein hydrolysate or of a combination of several protein hydrolysates or also are obtained by biotechnology processes and are present in the abovementioned ratios by weight.

Mention may in particular be made, among protein hydrolysates which can be used in the context of the present invention, of whey, casein, soy, gluten, barley and almond hydrolysate.

Thus, such hydrolysates can be mixed so as to obtain the desired ratios by weight of amino acids essential for the implementation of the present invention.

The processes for obtaining such hydrolysates of use in the cosmetics field are

known to a person skilled in the art.

According to one variant, it is possible, for example, to use a protein hydrolysate such as described in the process for obtaining stabilized 25% almond protein in water provided by Cognis.

Mention may be made, as process for obtaining such protein hydrolysates, of enzymatic hydrolysis.

In such a process, the protein substrates are brought together with enzymes, such as papain, pepsin or trypsin of animal, vegetable or microbial origin.

Such hydrolysates can also be enriched in one or more subsequent and/or associated stages.

The compositions according to the invention may be appropriate for administration by the oral route or for application by the topical route, or even for microinjection type, possibly associated with an ancillary experimental instrument capable of generating, for example, infrared radiation or ultrasound.

According to a specific variant, the compositions according to the invention can additionally comprise at least one of the compounds chosen from polyphenols, fatty acids, vitamins, such as vitamins B1, B3, B5, B6, B8, B12, C, D or PP, tocopherol (vitamin E) and its derivatives, in particular esters, such as tocopherol acetate or palmitate, zinc or its salts, selenium, niacin, a carotenoid, such as β-carotene, lycopene, zeaxanthin and lutein, polyunsaturated fatty acids, gelatin and seborrhoea regulators.

According to a specific variant, these active principles can be chosen from those which make it possible to improve the appearance of the hair; use may in particular be made of vitamin B6, cystein, vitamin B1 (biotin), vitamin B12 (bepanthen) and gelatin.

The oral compositions can additionally comprise an antioxidant complex comprising vitamins C and E and at least one carotenoid, in particular a carotenoid chosen from β-carotene, lycopene, astaxanthin, zeaxanthin and lutein, or flavonoids, such as catechins, hesperidine, proanthocyanidins, in particular in the form of blackcurrant seed oil, and anthocyanins.

The oral compositions can additionally comprise at least one probiotic, one prebiotic or a mixture of probiotics and a mixture of prebiotics. Mention may in particular be made, as probiotic microorganisms, of *Lactobacillus johnsonii* or *Lactobacillus paracasei*.

The compositions according to the second embodiment of the invention may be cosmetic or pharmaceutical compositions.

The compositions in accordance with the present invention, whether administered orally and/or topically, can be provided in all the formulation forms normally used, according to the method of administration concerned.

In the case of the oral route, the compositions in accordance with the present invention can be employed in a formulation of food supplement or functional food type, or alternatively of oral pharmaceutical composition type.

Typically, the duration of this cosmetic treatment can be greater than 4 weeks, in particular from 4 to 15 weeks, with, if appropriate, one or more periods of interruption.

More especially, the subject-matter of the present invention is a method for the cosmetic care of the hair and/or the scalp in women for the purpose of improving its condition and/or appearance of said hair and/or said scalp, characterized in that it consists in administering, by the oral route, a combination in accordance with the invention or a composition comprising it, in particular in the form of a food supplement or of a functional food, in particular with the active principles forming a combination in accordance with the present invention, which can be in the contents specified above, optionally combined with supplementary amino acids, peptides or peptide derivatives, as defined above.

Such compositions of food supplement or pharmaceutical composition type can be provided in particular in the form of soft capsules, hard gelatine capsules, banded gelatin capsules, gels, dry or liquid emulsions, tablets, powders to be diluted or phials to be taken orally or any other form known to the person skilled in the art.

The compositions can optionally comprise appropriate formulation excipients, such as a dye, sweetener, filler, binder, preservative, and the like.

According to a favoured variant, the active principles can be incorporated in food matrices for the purpose of producing functional foods, such as food bars, enriched foods, such as oils, margarines, compacted powders, fibres or also in the form of an emulsion in drinks.

The compositions can additionally comprise compounds, such as antioxidants, vitamins or minerals, authorized in Europe in food supplements as described in Directive 2002/46/EEC.

The food supplements in accordance with the present invention can comprise a

portion of the active principles forming a combination according to the invention in a first composition and the other portion of these active principles in a second composition, such as a kit or a combination product for a use which is simultaneous, separated or spread out over time.

This supplement can be formulated in such a way that the two compositions are in the same forms or in different forms, for example chosen from those mentioned above. Such a kit can in particular be presented in one and the same packaging.

For topical application on the hair, including the scalp, the compositions in accordance with the invention can have the form of an aqueous, alcoholic, aqueous/alcoholic or oily solution or suspension, of an emulsion or dispersion with a more or less fluid consistency and in particular a liquid or semi-liquid consistency, obtained by dispersion of a fatty phase in an aqueous phase (O/W) or vice versa (W/O), of an (O/W) or (W/O) solid dispersion or emulsion, of an aqueous, aqueous/alcoholic or oily gel which is more or less fluid or solid, of a free or compact powder to be used as is or to be incorporated in a physiologically acceptable medium, or also of microcapsules or microparticles, or of vesicular dispersions of ionic and/or nonionic type.

It is also possible to envisage compositions in the form of a foam or in the form of a spray or aerosol then comprising a pressurized propellant.

The compositions can be provided in the form of a lotion, serum, milk, O/W or W/O cream, gel, ointment, pomade, powder, balm, patch, impregnated pad, soap, cake or foam.

In particular, the compositions for application to the scalp or the hair can be provided in the form of a hair care lotion, for example for daily or twice-weekly application, of a shampoo or of a hair conditioner, in particular for twice-weekly or weekly application, of a liquid or solid soap for cleaning the scalp, for daily application, of a product for shaping the hairstyle (lacquer, hairsetting product, styling gel), of a hair mask, of a cream or of a foaming gel for cleaning the hair. They can also be provided in the form of a hair dye or mascara to be applied with a brush or comb.

According to a specific embodiment, the compositions according to the invention are provided in the form of a hair cream or lotion, of a shampoo, of a hair conditioner or of a hair mascara.

The amounts of the various constituents of the physiological medium of the compositions according to the invention are those generally used in the fields under consideration. In addition, these compositions are prepared according to conventional methods.

When the compositions are emulsions, the proportion of the fatty phase can range from 2% to 80% by weight and preferably from 5% to 50% by weight, with respect to the total weight of the composition. The aqueous phase is adjusted according to the content of fatty phase and of compound(s) (I) and according to the content of possible additional ingredients, in order to obtain 100% by weight. In practice, the aqueous phase represents from 5% to 99.9% by weight.

The fatty phase can comprise fatty or oily compounds which are liquid at ambient temperature (25°C) and atmospheric pressure (760 mmHg), generally known as oils. These oils may or may not be compatible with one another and may form a macroscopically homogeneous liquid fatty phase or a two- or three-phase system. In addition to these oils, the fatty phase can comprise waxes, gums, lipophilic polymers, or "pasty" or viscous products comprising solid parts and liquid parts.

The aqueous phase comprises water and optionally an ingredient miscible in any proportion with water, such as lower C_1 to C_8 alcohols, for example ethanol or isopropanol, polyols, such as propylene glycol, glycerol or sorbitol, or else acetone or ether.

The emulsifiers and coemulsifiers used to produce a composition in the form of an emulsion are those generally used in the cosmetics field. In addition, their nature depends on the sense of the emulsion. In practice, the emulsifier and optionally the coemulsifier are present in the composition in a proportion ranging from 0.1% to 30% by weight, preferably from 0.5 to 20% by weight and better still from 1 to 8%. In addition, the emulsion can comprise lipid vesicles and in particular liposomes.

When the compositions are in the form of an oily solution or gel, the fatty phase can represent more than 90% of the total weight of the composition.

Advantageously, the compositions are aqueous, alcoholic or aqueous/alcoholic solutions or suspensions and better still water/ethanol solutions or suspensions. The alcohol fraction can represent from 5% to 99.9% and better still from 8% to 80%.

For a mascara application, the compositions are in particular wax-in-water or

wax-in-oil dispersions, gelled oils or aqueous gels. They may or may not be pigmented.

The compositions of the invention can comprise, in addition, other ingredients generally used in the fields concerned chosen from solvents, thickeners or gelling agents for the aqueous phase or for the oily phase, colouring materials which are soluble in the medium of the composition, solid particles of the filler or pigment type, antioxidants, preservatives, fragrances, electrolytes, neutralizing agents, UV-blocking agents, such as sunscreens, film-forming polymers, cosmetic active principles with a beneficial effect on the skin or keratinous fibres, or their mixtures. These additives can be present in the compositions according to the amounts generally used in the cosmetic and dermatological fields and in particular in a proportion of 0.01 to 50% of the total weight of the composition and better still of 0.1 to 20% and, for example, of 0.1 to 10%. These adjuvants, depending on their nature, can be introduced into the fatty phase, into the aqueous phase and/or into the lipid vesicles and in particular liposomes.

Of course, a person skilled in the art will take care to choose the possible supplementary additives and/or their amounts so that the advantageous properties of the compositions according to the invention are not, or not substantially, detrimentally affected by the envisaged addition.

Mention may be made, as solvents which can be used in the invention, of lower C_2 to C_8 alcohols, such as ethanol or isopropanol, propylene glycol and certain light cosmetic oils, such as C_6 to C_{16} alkanes.

Mention may be made, as oils which can be used in the invention, of oils of mineral origin (liquid petrolatum, hydrogenated isoparaffin), oils of vegetable origin (liquid fraction of shea butter, sunflower oil, apricot oil, soybean oil, fatty alcohol or fatty acid), oils of animal origin (perhydrosqualene), synthetic oils (fatty acid esters, purcellin oil), silicone oils (phenyltrimethicones, linear or cyclic polydimethylsiloxanes) and fluorinated oils (perfluoropolyethers). Mention may be made, as waxes, of silicone waxes, beeswax, candelilla wax, rice wax, carnauba wax, paraffin wax or polyethylene wax.

Mention may be made, as emulsifiers which can be used in the invention, of, for example, glyceryl stearate or laurate, sorbitol stearates or oleates, alkyl dimethicone copolyols (with alkyl ≥ 8) and their mixtures for a W/O emulsion. Use may also be made of polyethylene glycol monostearate or monolaurate, polyoxyethylenated sorbitol stearate or oleate, dimethicone copolyols and their mixtures for an O/W emulsion. The emulsifier

and the coemulsifier are present in the compositions in a proportion ranging from 0.3 to 30% by weight and preferably from 0.5 to 20% by weight, with respect to the total weight of the composition.

Mention may be made, as hydrophilic gelling agents which can be used in the invention, of carboxyvinyl polymers (carbomer), acrylic copolymers, such as acrylate/alkylacrylate copolymers, polyacrylamides, polysaccharides, such as hydroxypropylcellulose, natural gums and clays and mention may be made, as lipophilic gelling agents, of modified clays, such as bentones, metal salts of fatty acids, such as aluminium stearates, hydrophobically treated silica, ethylcellulose or their mixtures.

The compositions can comprise, as cosmetic active principle other than the combinations of active principles in accordance with the invention, an additional hydrophilic active principle chosen from polyols, urea, allantoin, sugars and sugar derivatives, water-soluble vitamins, plant extracts (those of Iridaceae or of soya) and hydroxy acids (fruit acid or salicylic acid); and/or an additional lipophilic active principle chosen from retinol (vitamin A) and its derivatives, in particular esters (retinol palmitate), essential fatty acids, ceramides, essential oils, salicylic acid derivatives, such as 5-(n-octanoyl)salicylic acid, esters of hydroxy acids, phospholipids, such as lecithin, or their mixtures.

According to a specific embodiment of the invention, it is possible to combine, with the combinations of active principles in accordance with the invention, at least one additional compound which promotes the regrowth and/or which limits the loss of the hair. These additional compounds are chosen in particular from lipoxygenase inhibitors, such as described in EP 0 648 488, bradykinin inhibitors, described in particular in EP 0 845 700, prostaglandins and their derivatives, in particular those described in WO 98/33497, WO 95/11003, JP 97-100091 or JP 96-134242, prostaglandin receptor agonists or antagonists, nonprostanoic prostaglandin analogues, such as described in EP 1 175 891 and EP 1 175 890, WO 01/74307, WO 01/74313, WO 01/74314, WO 01/74315 or WO 01/72268, or their mixtures.

Mention may be made, as other additional compounds which promote the growth of the hair which can be present in the compositions according to the invention, of vasodilators, antiandrogens, cyclosporins and their analogues, antimicrobials and antifungals, anti-inflammatories or retinoids, alone or as a mixture.

The vasodilators which can be used are in particular potassium channel agonists, including minoxidil, cromakalim, nicorandil and diazoxide, alone or in combination.

The antiandrogens which can be used include in particular steroidal or nonsteroidal inhibitors of 5α-reductase, such as finasteride, cyprosterone acetate, azelaic acid, its salts and its derivatives, flutamide, oxendolone, spironolactone or diethylstilbestrol.

The antimicrobial or antifungal compounds can be chosen from selenium derivatives, octopirox, triclocarban, triclosan, zinc pyrithione, itraconazole, asiatic acid, hinokitiol, mipirocin, tetracyclines, in particular erythromycin, clinycin hydrochloride, benzoyl peroxide or benzyl peroxide, minocyclin and the compounds belonging to the class of the imidazoles, such as econazole, ketoconazole or miconazole or their salts, or nicotinic acid esters, including in particular tocopherol nicotinate, benzyl nicotinate and C_1-C_6 alkyl nicotinates, such as methyl nicotinate or hexyl nicotinate.

The anti-inflammatories can be chosen from steroidal anti-inflammatories, such as glucocorticoids or corticosteroids (for example: hydrocortisone), and nonsteroidal anti-inflammatories, such as glycyrrhetinic acid and α-bisabolol, benzydamine or salicylic acid.

The retinoids can be chosen from isotretinoin, acitretin and tazarotene.

Mention may be made, as other additional active compounds for promoting the growth and/or limiting the loss of the hair which can be used in combination with the combinations of active principles in accordance with the present invention, of aminexil, 6-O-[(9Z,12Z)-octadeca-9,12-dienoyl]hexapyranose, benzalkonium chloride, benzethonium chloride, phenol, oestradiol, chlorpheniramine maleate, chlorophyllin derivatives, cholesterol, cysteine, methionine, menthol, peppermint oil, calcium pantothenate, panthenol, resorcinol, protein kinase C activators, glycosidase inhibitors, glycosaminoglycanase inhibitors, pyroglutamic acid esters, hexosaccharidic acid or acylhexosaccharic acid, aryl-substituted ethylenes, N-acylated amino acids, flavonoids, ascomycin derivatives and analogues, histamine antagonists, saponins, proteoglycanase inhibitors, oestrogen agonists and antagonists, pseudopterins, cytokines and growth factor promoters, IL-1 or IL-6 inhibitors, IL-10 promoters, TNF inhibitors, benzophenones and hydantoin, retinoic acid; vitamins, such as vitamin D, analogues of vitamin B12 and

pantothenol; triterpenes, such as ursolic acid; antipruritic agents, such as thenaldine, trimeprazine or cyproheptadine; agents for combating parasites, in particular metronidazole, crotamiton or pyrethroids; calcium antagonist agents, such as cinnarizine, diltiazem, nimodipine, verapamil, alverine and nifedipine; hormones, such as oestriol or its analogues, thyroxine and its salts, or progesterone; FP receptor (receptor to prostaglandins of the F type) antagonists, such as latanoprost, bimatoprost, travoprost or unoprostone; 15-hydroxyprostaglandin dehydrogenase inhibitors; their mixtures.

It is also possible to envisage that the compositions comprising at least a combination of active principles in accordance with the present invention are in the liposomed form. Thus, the combinations of active principles in accordance with the invention encapsulated in the liposomes can be delivered selectively to the hair follicle.

The compositions to which the invention applies can be applied to the hair or the scalp of an individual and can optionally be left in contact for several hours and can optionally be rinsed out.

It is possible, for example, to apply the compositions comprising an effective amount of a combination of active principles in accordance with the invention in the evening, to keep this composition in contact overnight and optionally to shampoo in the morning. These applications can be repeated daily for one or more months, depending on the individual.

Other characteristics and advantages of the invention will emerge better from the examples which follow, given by way of illustration and without implied limitation.

EXAMPLE 1 : Characterization of a profile of free amino acids in a healthy woman vs. a woman exhibiting a deficiency correlated with hair ageing and more particularly a detrimental change in the quality of the hair

1.1. Hair extraction protocol

The study was carried out on 71 subjects (35 young nonalopecic women and 36 elderly nonalopecic women). “Elderly” should be understood as meaning a population aged from 50 to 65 years and “young” should be understood as meaning a population aged from 20 to 35 years.

The individual hairs, to the number of 10 per individual, are withdrawn both from the nape and from the vertex.

The roots are homogenized in a microgrinder comprising sterile water. The samples are stored at -20°C before analysis according to the protocol described below.

1.2. Protocol for determining the amino acid, peptide and peptide derivative profile

Taurine and the free amino acids were determined on the Hitachi L-8800 amino acid autoanalyser by ion exchange chromatography.

PRINCIPLE OF THE ANALYSIS OF THE AMINO ACIDS:

The natural amino acids, some of their metabolites and small peptides (in particular glutathione) are separated on a column filled with a cation-exchange resin.

Elution is carried out as a function of the gradual increase in the pH and in the ionic strength of the eluants, and also of the variation in the temperature of the column.

A post-column reaction with ninhydrin is subsequently deployed at 135°C, thus giving a crimson coloration with all the amino acids, except with proline and its derivatives, which give a yellow coloration.

A colorimeter makes it possible to detect the amino acids at two wavelengths, 570 nm for all the amino acids except proline and its derivatives, which can be detected at 440 nm.

The duration of an analysis is composed of three cycles: a cycle of elution of the different amino acids (105 minutes), a cycle of rinsing (15 minutes) and then a cycle of equilibration of the column (30 minutes).

The following ready-for-use reactants were used: a standard commercial solution of amino acids from Sigma, asparagine (Sigma, ref.: 70-47-3), glutamine (Sigma, ref.: 56-85-9), reduced glutathione (Fluka, ref.: 70-18-8), oxidized glutathione (Fluka, ref.: 27025-41-8), O-Phospho-L-serine (Sigma, ref.: 407-41-0), O-Phosphorylethanolamine (Sigma, ref.: 1071-23-4), 1N hydrochloric acid and a ninhydrin/buffer kit (Hitachi, ref.: 142-05051).

A lithium citrate buffer solution, pH 2, 0.07M, was prepared from 10 g of citric acid monohydrate and 1.26 g of lithium hydroxide made up to 1000 ml with water, the said

solution having been subsequently adjusted with hydrochloric acid in order to obtain a pH of 2.

Elution buffers are prepared:

	Buffer 1	Buffer 2	Buffer 3	Buffer 4	Buffer 5
Distilled water	700 ml	700 ml	700 ml	700 ml	700 ml
Lithium citrate	5.73g	9.80 g	8.79 g	9.80 g	
Lithium hydroxide					8.40 g
Lithium chloride	1.24 g	6.36 g	26.62 g	38.15 g	
Citric acid	19.90 g	12.00 g	11.27 g	3.3 g	
Ethanol	30 ml	30 ml	100 ml		30 ml
Benzyl alcohol			3 ml		
2,2'-Thiodiethanol	5 ml	5 ml			
Brij 35	4 ml	4 ml	4 ml	4 ml	4 ml
Caprylic acid	0.1 ml	0.1 ml	0.1 ml	0.1 ml	0.1 ml
Total	1000 ml	1000 ml	1000 ml	1000 ml	1000 ml
Li^+ concentration	0.09	0.255	0.721	1	0.2
pH	2.8	3.7	3.4	4.1	

Post-column reactants of ready-for-use ninhydrin/buffer mixture type are available from ScienceTec (14205051).

The compositions and their use are described below.

	STAGES	REACTANTS	AMOUNTS
Ninhydrin	1	1-Methoxy-2-propanol	978.5 ml
	2	Ninhydrin	38.5 g
	3	Degassing operation via an inert gas	5 minutes
	4	Sodium borohydride	80.5 mg
	5	Degassing operation via an inert gas	5 minutes
Buffer	1	Distilled water	671 ml
	2	Lithium acetate	407 g
	3	Acetic acid	245 ml
	4	1-Methoxy-2-propanol	801 ml
	5	Degassing operation via an inert gas	10 minutes

The amino acid standard solutions are as follows:

1) Sigma commercial standard at 0.05 µmol/ml + O-phospho-L-serine and O-phosphorylethanolamine at 0.05 µmol/ml: (standard 1 comprising 40 amino acids).

This solution is stored at 4°C.

2) 0.05 µmol/ml standard solution of glutamine/asparagine/reduced glutathione/oxidized glutathione: (standard 2).

This solution must be prepared at the time of use.

The standard solutions (1 and 2) are dissolved in a pH 2 buffer, which makes it possible to positively charge the amine functional groups, and are then filtered through a 0.45 µm Millex filter into 2 ml vials.

The assay is prepared as follows:

The samples described above are gradually defrosted at 4°C.

The tubes are vortexed and centrifuged. An amount of supernatant of between 50 and 80 µl is withdrawn using a precision micropipette and transferred into 100 µl inserts.

ANALYSIS – QUANTITATIVE DETERMINATION

Chromatographic conditions:

The column is filled with cationic resin (Hitachi 2622SC) with a length of 60 mm and a diameter of 4.6 mm. It is, beforehand, conditioned and regenerated in the Li^+ form with the eluant buffer 5.

Elution is carried out according to the programme reported in Table 1 below.

The volume injected is 25 µl for the standard solutions.

The volume of the samples injected can vary according to the volume of the supernatant recovered (a margin of 20 µl is necessary at any injection in view of the structure of the sampling needle).

TABLE 1: Programme for elution on the Hitachi L8800 amino acid analyser:

STAGES	TIME (minutes)	ELUTION BUFFERS (total 100%)					COLUMN TEMPERATURE (°C)	FLOW RATE (ml/min)	
		1	2	3	4	5		Eluant pump	Ninhydrin/Buffer pump
1	0	100					38	0.35	0.35
2	10	"					30	"	"
3	17.9	"					"	"	"
4	18	80	20				"	"	"
5	20.5	"	"				52	"	"
6	29.5	70	30				"	"	"
7	31.6	10	90				"	"	"
8	39	"	"				45	"	"
9	43	"	"				"	"	"
10	43.1		100				"	"	"
11	51		"				70	"	"
12	51.1			100			"	"	"
13	67			"			45	"	"
14	73			"			"	"	"
15	73.1				100		"	"	"
16	92				"		70	"	"
17	107				"		"	"	"
18	107.1					100	"	"	"
19	112					"	"	"	"
20	120					"	38	"	"
21	120.1	100					"	"	"
22	122	"					"	"	"
23	150	"					"	"	"

REACTION TEMPERATURE
NINHYDRIN: 135°C

Quantitative determination:

Quantitative determination is carried out by external calibration using the amino acid standard solutions 1 and 2. From the viewpoint of the satisfactory reproducibility of the post-column colorimetric method, the calibration straight line for each amino acid is composed of the value of a point of the range and of that corresponding to the analysis of a blank (straight line passing through the origin).

Nevertheless, standards are prepared once weekly for standard 1 and at the time of use for standard 2 and are injected every 8 samples in order to monitor the reliability of the results.

The amount of each amino acid present is calculated after integrating the Visible signal and is given as relative content.

1.3. Profile of free amino acids in a healthy woman vs. a woman exhibiting a deficiency correlated with hair ageing and more particularly a detrimental change in the quality of the hair

A Table 2 is reported below, giving the values of amino acids, peptides or peptide derivatives analysed respectively for the two populations analysed. The values are reported therein as molar percentage, with respect to the total amount of the material analysed, of amino acids, peptides and peptide derivatives.

TABLE 2

	Elderly nonalopecic women	**Young nonalopecic women**
Glutamic acid	10.3%	12.0%
Reduced glutathione	9.0%	10.5%
Threonine	2.7%	3.0%

From the comparison of these aminograms, it emerges that a deficiency in glutamic acid, reduced glutathione and threonine is observed in elderly women in comparison with young women. A reduction in the content is also observed for some other amino acids but at a less significant scale.

Example 2: Characterization of a free amino acid profile in a healthy woman versus a woman having a deficiency correlated with a hair disorder, and more particularly alopecia

2.1. Hair extraction protocol

The study was carried out on 107 individuals (36 elderly women without alopecia and 71 elderly women with alopecia). The term "elderly" should be understood to mean a population with an age of 50 to 65.

10 hairs per individual are removed both from the nape of the neck and from the vertex.

The roots are homogenized in a micromill containing sterile water. The samples are stored at -20°C before analysis according to the protocol as above-described.

2.2. Protocol for determining the amino acid, peptide and peptide derivative profile

The taurine and the free amino acids were determined according to the above-described protocol in example 1, 1.2..

2.3. Free amino acid profile in normal women versus a woman having a deficiency correlated with a hair disorder, and more particularly alopecia

A Table 3 is reported below, giving the values of amino acids, peptides or peptide derivatives, analysed respectively for the two populations analysed.

The values are reported as molar percentage relative to the total amount of amino acids, peptides and peptide derivatives, as reported in Table 3 below, forming the material analysed.

TABLE 3

	Elderly women with alopecia	**Eldery women without alopecia**
Glutamine	6.9%	9.1%
Reduced glutathione	6.0%	9.0%
Leucine	1.9%	2.2%
Asparagine	0.6%	1.4%
Tyrosine	1.0%	1.2%

From the composition of the two aminograms, it emerges that a deficiency in glutamine, reduced glutathione, leucine, asparagine and tyrosine is observed in the elderly women compared with the young women. A decrease in the contents for certain other amino acids is also observed, but on a less significant scale.

Example 3: Compositions

- Hair lotion

Components	Amount (% w/w)
Fragrance	0.2
Reduced glutathione or Cystine (Reduced glutathione precursor)	0.9
Threonine	0.2
Glutamic acid	1
PEG-40 hydrogenated castor oil	0.2
Alcohol denat.	16.2
Water	81.3
Total	100

- Hair lotion

Components	Amount (% w/w)
Fragrance	0.2
Reduced glutathione or Cystine (Reduced glutathione precursor)	1
Glutamine	1
Leucine	0.3
Asparagine	0.024
Tyrosine	0.2
PEG-40 hydrogenated castor oil	0.2
Alcohol denat.	16.2
Water	80.876
Total	100

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CLAIMS

1. Cosmetic use, by the oral and/or topical route, of a combination of reduced glutathione or one of its antioxidant analogues or precursors and two or more amino acids chosen from glutamic acid, threonine, glutamine, leucine, asparagine and tyrosine for improving the quality and/or preventing and/or treating a detrimental change in the quality of the hair in women.

2. Use according to claim 1 of a combination of glutamic acid, reduced glutathione or one of its antioxidant analogues or precursors and threonine for preventing and/or treating weak, brittle, lifeless or thinned hair, preventing and/or treating split ends, improving the softness and the strength of the fibre or improving the volume of the hair and its sheen in women.

3. Use according to claim 1 or 2, in which reduced glutathione, glutamic acid and threonine are employed in amounts such that the amount of glutamic acid is greater than the amount of glutathione and this amount is itself greater than the amount of threonine.

4. Use according to claim 2 or 3, characterized in that the ratio by weight of reduced glutathione to glutamic acid is between 0.1 and 1.5, in particular between 0.5 and 1 and more particularly between 0.6 and 0.9.

5. Use according to any one of claims 2 to 4, characterized in that the ratio by weight of threonine to glutamic acid is between 0.07 and 0.4, in particular between 0.1 and 0.3 and more particularly between 0.15 and 0.25.

6. Use according to any one of claims 2 to 5, characterized in that the said combination is formulated in a composition additionally comprising at least one of the amino acids, peptides or peptide derivatives chosen from the group consisting of taurine, glutamine, glycine and optionally aspartic acid, serine and alanine.

7. Use according to any one of claims 2 to 6, characterized in that the said composition additionally comprises taurine, glutamine, glycine and optionally aspartic acid, serine and alanine and in that the ratios by weight of glutamine and glycine, taken independently, to taurine are between 0.2 and 0.6, in particular between 0.3 and 0.5; the ratios by weight of aspartic acid, serine and alanine, taken independently, to taurine are between 0.1 and 0.5, preferably between 0.2 and 0.4; the ratio by weight of glutamic acid

to taurine is greater than 0.6; the ratio by weight of reduced glutathione to taurine is greater than 0.4; and/or the ratio by weight of threonine to taurine is greater than 0.1.

8. Use according to any one of claims 2 to 7, characterized in that the said combination or composition comprising it can be applied by the topical route and in that the content of glutamic acid is between 2 and 12% by weight of the composition, in particular between 5 and 10% by weight and more particularly still between 6 and 8% by weight, with respect to the total weight of the composition.

9. Use according to claim 1 of a combination of reduced glutathione or an antioxidant precursor or analogue thereof, of glutamine, of leucine, of asparagine and of tyrosine, for preventing and/or treating hair loss and/or alopecia in women.

10. Use according to claim 1 or 9, characterized in that the reduced glutathione, or an antioxidant precursor or analogue thereof, the glutamine, the leucine, the asparagine and the tyrosine are used in respective amounts such that the amounts of reduced glutathione, or an antioxidant precursor or analogue thereof, and glutamine are equivalent and greater than the amount of leucine, the latter being greater than the amount of asparagine, which is itself equal to the amount of tyrosine.

11. Use according to claim 9 or 10, characterized in that the ratio by mass between glutamine and reduced glutathione is between 0.5 and 1.5, in particular between 0.7 and 1.3, and more particularly between 0.9 and 1.1.

12. Use according to any one of claims 9 to 11, characterized in that the ratio by mass between leucine and reduced glutathione is between 0.07 and 0.7, in particular between 0.1 and 0.5, and more particularly between 0.2 and 0.4.

13. Use according to any one of claims 9 to 12, characterized in that the ratio by mass between asparagine and tyrosine, taken independently, and reduced glutathione is between 0.05 and 0.3, in particular between 0.07 and 0.2, and more particularly between 0.09 and 0.15.

14. Use according to any one of claims 9 to 13, characterized in that said combination is used in the form of a composition comprising, in addition, at least one supplementary amino acid, peptide or peptide derivative chosen from the group constituted of taurine, glutamic acid, glycine, aspartic acid, serine and alanine.

15. Use according to any one of claims 9 to 14, characterized in that said composition also contains taurine, glutamic acid, glycine, and optionally aspartic acid,

serine and alanine, and in that the ratio by mass between glutamic acid and taurine is between 0.4 and 0.8, preferably between 0.5 and 0.7; the ratio by mass between glycine and taurine is between 0.2 and 0.6, preferably between 0.3 and 0.5; the ratios by mass between aspartic acid, serine and alanine, taken independently, and taurine are between 0.1 and 0.5, preferably between 0.2 and 0.4; the ratios by mass between glutamine and reduced glutathione, taken independently, and taurine are greater than 0.4; the ratio by mass between leucine and taurine is greater than 0.3 and/or the ratio by mass between asparagine and tyrosine is greater than 0.1.

16. Use according to any one of claims 1 and 9 to 15, characterized in that said combination or composition containing same can be applied topically, and in that the content with respect to reduced glutathione, or reduced glutathione equivalent, is between 2% and 12% by weight of the composition, in particular between 5% and 10% by weight, and even more particularly between 6% and 8% by weight, relative to the total weight of the composition, as reduced glutathione equivalent by mass.

17. Use according to any one of the preceding claims, characterized in that the said combination or composition comprising it is intended for topical application and in that it is provided in the form of an aqueous, alcoholic, aqueous/alcoholic or oily solution or suspension, of an emulsion or dispersion with a more or less fluid consistency and in particular a liquid or semi-liquid consistency, obtained by dispersion of a fatty phase in an aqueous phase (O/W) or vice versa (W/O), of an (O/W) or (W/O) solid dispersion or emulsion, of an aqueous, aqueous/alcoholic or oily gel which is more or less fluid or solid, of a free or compact powder to be used as is or to be incorporated in a physiologically acceptable medium, or also of microcapsules or microparticles, or of vesicular dispersions of ionic and/or nonionic type, or in the form of a foam, spray or aerosol, or also of a lotion, serum, milk, O/W or W/O cream, gel, ointment, pomade, powder, balm, patch, impregnated pad, soap, cake or foam.

18. Use according to any one of claims 1 to 7 and 9 to 15, characterized in that the said combination or composition comprising it is provided in the form of a food supplement, in particular in the form of soft capsules, hard gelatin capsules, banded gelatin capsules, gels, dry or liquid emulsions, tablets, powders to be diluted or phials to be taken orally, or of an enriched food.

19. Use according to any one of claims 1 to 7 and 18, characterized in that said

combination or composition containing same is intended for oral administration, and in that it contains from 10 to 300 mg of glutamic acid, especially from 20 to 200 mg, in particular from 30 to 170 mg.

20. Use according to any one of claims 2 to 7, 18 and 19, characterized in that glutamic acid is administered in a proportion of a content of 30 to 300 mg/day, in particular of 50 to 200 mg/day, more particularly still of between 80 to 180 mg/day and in particular between 120 and 170 mg/day.

21. Use according to any one of claims 1, 9 to 15 and 18, characterized in that said combination or composition containing same is intended for oral administration, and in that it contains from 10 to 300 mg of reduced glutathione or reduced glutathione equivalent, especially from 20 to 200 mg, in particular from 30 to 170 mg.

22. Use according to any one of claims 1, 9 to 15, 18 and 21, characterized in that the reduced glutathione, or an antioxidant precursor or analogue thereof, is administered at a content of from 30 to 300 mg/day, in particular from 50 to 200 mg/day, even more particularly from 80 to 180 mg/day, and especially between 120 and 170 mg/day, with respect to reduced glutathione or reduced glutathione equivalent by mass.

23. Use according to any one of the preceding claims, characterized in that the combination is employed in the form of a composition additionally comprising at least one of the compounds chosen from polyphenols, fatty acids, vitamins, such as vitamins B1, B3, B5, B6, B8, B12, C, D or PP, tocopherol and its derivatives, in particular esters, such as tocopherol acetate or palmitate, zinc or its salts, selenium, niacin, a carotenoid, such as β-carotene, lycopene, zeaxanthin and lutein, polyunsaturated fatty acids, gelatin and seborrhoea regulators.

24. Use according to any one of the preceding claims, characterized in that the amino acids, peptides and peptide derivatives are employed in the form of a protein hydrolysate or of combinations of several protein hydrolysates or also are obtained by biotechnology processes.

25. Cosmetic or pharmaceutical composition comprising, as sole amino acids, glutamic acid and threonine in combination with reduced glutathione or one of its antioxidant analogues or precursors.

26. Composition according to claim 25, in which the combination is as defined in claims 3 to 5, 8, 17 to 20, 23 and 24.

27. Cosmetic or pharmaceutical composition comprising, as sole amino acids, glutamine, leucine, asparagine and tyrosine in combination with reduced glutathione or an antioxidant precursor or analogue thereof.

28. Composition according to claim 27, in which the combination is as defined in claims 10 to 13, 16 to 18 and 21 to 24.

29. Method for the cosmetic treatment of the hair in women which is intended to improve the quality of the hair and/or hair fibres, characterized in that it comprises at least the administration by the oral route or the topical application of a combination according to any one of claims 1 to 8, 17 to 20 and 23 to 24.

30. Method for cosmetic treatment of the hair in women, including the scalp, intended to stimulate hair growth in women and/or prevent and/or reduce hair loss, characterized in that it comprises at least the oral administration or the topical application of a combination according to any one of claims 1, 9 to 18 and 21 to 24.

INTERNATIONAL SEARCH REPORT

International application No
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A. CLASSIFICATION OF SUBJECT MATTER
INV. A61Q5/00 A61K8/44 A61K8/64 A61Q7/00
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)
A61Q A61K

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

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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

* Special categories of cited documents :

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Date of the actual completion of the international search	Date of mailing of the international search report
22 April 2010	04/05/2010

Name and mailing address of the ISA/	Authorized officer
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