



\*159159\*



\*G00002\*

**Slimming cosmetic composition containing a substance  
inducing the production of IL-6**

The present invention relates to cosmetic  
5 compositions containing slimming active substances.

The active substances present in the cosmetic  
composition are chosen from an antagonist of the  
receptors for neuropeptide Y called hereinafter NPY, an  
antagonist of the  $\alpha 2$  receptors and an inducer of the  
10 production of interleukin-6 called hereinafter IL-6.

The NPY antagonist, the  $\alpha 2$  antagonist or the  
inducer of the production of IL-6 may be a nonpeptide  
compound, a peptide, a cell or tissue extract of animal  
or plant origin or a product obtained by fermentation  
15 by a microorganism, for example a bacterium or a  
fungus.

Patent application EP 838217 describes a  
slimming cosmetic composition which contains an NPY  
antagonist and an  $\alpha 2$  antagonist. The active substances  
20 in this composition are obtained by fermentation by two  
microorganisms deposited at the C.N.C.M. of Institut  
Pasteur where they were registered under the references  
I 1332 and I 1778, respectively. In the present  
description, these active substances will be called  
25 substance A and substance B, respectively. The slimming  
cosmetic composition containing them will be called  
composition Am1.

This slimming composition Am1 acts on the subcutaneous adipose tissue and controls the release of the fat stored in the adipocytes.

By blocking the  $\alpha 2$  and NPY receptors, composition Am1 makes it possible to clear the hypertrophied adipocytes and to avoid any new excessive adipocyte storage by allowing the expression of the  $\beta$  receptors whose prolipolytic activity is normally masked by the antilipolytic  $\alpha 2$  and NPY receptors which are largely in excess in the subcutaneous adipose tissues. Composition Am1 thus makes it possible to act effectively on the outflow of the fatty acids stored in the adipocytes.

The compositions according to the present invention maintain this activity but supplement it, on the one hand, by a retarding action on the entry of fatty acids which exerts itself by a reducing effect on the production of LPL, the enzyme responsible for the entry of fatty acids into the cell and, on the other hand, on the hyperplasia of the adipocytes. This unexpected supplementary effect is obtained by a substance capable of inducing the production of IL-6 by the adipocytes. This substance is produced by a microorganism deposited at the C.N.C.M. of Institut Pasteur registered under the reference I 1844. This active substance will be called hereinafter substance C.

For long considered solely for their role as energy reserve, the adipocytes have demonstrated during the past few years endocrine and secretory cell functions (Ailhaud G. et al. Médecine/Science 1998, 14, 858-864). Leptin perfectly illustrates this new secretory function of the adipocyte. This protein is specifically produced by the mature adipocyte. It is involved in controlling satiety; it is also thought to be involved in the regulation of fatty deposits. The adipocyte is thus responsible for the production of factors with autocrine and paracrine activity which will modulate the physiology of the adipose tissue.

In particular, it has been very recently demonstrated that the endocrine function of the adipocyte is exerted on two specific mediators:

- lisophosphatidic acid (LPA), a lipid factor whose production is mediated by the activation of the  $\alpha 2$  receptor and whose function consists in recruiting new adipocytes (Valet P. et al. J. Clin. Invest. 1998, 101(7), 1431-1438).

- IL-6, which is a multifunctional cytokine.

Substance C is known as an inducer of the production of IL-6 by the keratinocytes. Its method of production is described in international patent application WO 99/40896. It exerts an effect on skin ageing.

Nothing could indicate that this substance (produced by the microorganism I 1844) would moreover have exerted a double action on the adipocytes.

Recently, studies have shown that the adipose  
5 cells could produce IL-6 whose function at the adipocyte level consists in repressing the synthesis of LPL, the enzyme responsible for the entry of fatty acids into the adipose cell (Greenberg A.S. *et al.* Cancer Research 1992, 52, 4113-4116).

10 The production of IL-6 by the cells of the subcutaneous adipose tissue is positively correlated with an increase in the body mass index (Mohamed Ali V. *et al.* J. Clin. Endocrinol. Metab. 1997, 82, 4196-4200) but also differs according to the origin of the adipose  
15 tissue.

Thus, in obese subjects, the basal adipocytes collected from the omental region releases 2 to 3 times more IL-6 than the subcutaneous adipocytes (Fried S.K. *et al.* J. Clin. Endocrinol. Metab. 1998, 83, 847-860).

20 Finally, in addition to the capacity of IL-6 to reduce the production of LPL by the adipocytes, IL-6 could also act, through inhibition, on the differentiation of the adipocyte-precursor cells (Hauner H. *et al.* 8th International Congress on Obesity  
25 1999, 47-53).

IL-6 therefore appears as a cytokine which has an autocrine action (on LPL) and a paracrine action

(on the preadipocytes) for slowing down the development of the subcutaneous adipose tissue.

However, like all cytokines, IL-6 is a pleiotropic glycoprotein, that is to say that it exhibits different effects depending on the cell producing it. Thus, at the level of the adipocyte, IL-6 will have effects of a completely different type to those already known with the keratinocyte.

In particular, in the adipocyte, the IL-6 synthesized by the cell down-regulates the content and therefore the activity of the enzyme which is responsible for the entry of fats.

Thus, the compositions according to the invention make it possible to control the phenomena of entry and outflow of fatty acids including storage and hypertrophy of the adipocytes. It also makes it possible to act on adipocyte hyperplasia.

It is known that the formation of new adipocytes occurs in humans throughout the life of the individuals. Thus, "dormant" fatty cells have been isolated in elderly subjects whatever their gender (Ailhaud G. *et al.* *Int. J. Obes. Relat. Metab. Disord.* 1992, 16(2), 517-521; Spiegelman B *et al.* *Cell* 1996, 87, 377-389; Hauner *et al.* *J. Clin. Invest.* 1989; 84, 1663-1670).

The development of the adipose tissue results from an increase in the size of the adipocytes following the excessive accumulation of fatty acids, as

well as from the recruitment of new fatty cells obtained from the multiplication and differentiation of adipocyte-precursor cells, the preadipocytes (Valet P. et al. J. Clin. Invest. 1998, 101(7), 1431-1438).

5                This recruitment of new adipocytes is mediated by soluble factors produced by the hypertrophied adipocytes: in particular by LPA via the stimulation of the  $\alpha 2$  receptor, and by IL-6 via its controlling power on preadipocyte differentiation.

10              The blocking of the  $\alpha 2$  receptor is therefore such as to allow, in parallel with its beneficial effect on lipolysis, repression of the release of LPA, with, as advantage, an inhibition of the recruitment of new adipocytes.

15              IL-6 limits the maturation of the preadipocytes into differentiated adipocytes. The adipocyte stimulation of the production of this cytokine by the inducer of IL-6 reinforces this property.

20              The combination of substance B, inhibitor of the receptor, and of substance C, inducer of IL-6, is therefore such as to allow an increased and innovative efficacy on the hyperplasia of the fatty cells. The addition of substance A to this combination makes it  
25 possible to obtain a slimming composition which acts on several mechanisms of action, namely hypertrophy and hyperplasia.

Studies have been carried out to demonstrate the activity of the active substance obtained from the microorganism I 1844, or substance C, on the mature adipocytes and on the adipocyte differentiation.

5           A slimming cosmetic composition has now been prepared, according to the invention, which contains substances A, B and C and which will be called hereinafter Am2.

          The slimming effect of Am2 has been the  
10   subject of clinical studies.

          The biological effects of substance C *in vitro* has been studied on the murine line 3T3-L1. This preadipocyte line, routinely cultured in DMEM medium (Dubelco's Minimum Essential Medium) enriched with 10%  
15   foetal calf serum has the property of differentiating into mature adipocytes in the presence of inducers such as insulin and indomethacin (Slieker L. J. Biochem. Biophys. Res. Com. 1998, 251, 225-229). Eight to ten days after the induction of differentiation, the 3T3-L1  
20   cells exhibit the characteristics of mature adipocytes. This passage from the stage of immature cell to the stage of functional adipocyte can be morphologically assessed by the appearance of intracytoplasmic lipid storage vesicles which are visible under the microscope  
25   or which can be biochemically detected by measuring the production of leptin, the hormone for satiety produced solely by mature adipocytes.

The influence of substance C on the adipocyte activity was evaluated at two levels. On the one hand, by measuring the capacity of this active agent to modulate the production of adipocyte IL-6 and, on the other hand, by evaluating its effect on differentiation into mature adipocytes.

**1- Effect of substance C on the production of IL-6 by the mature adipocytes 3T3-L1**

Mature adipocytes 3T3-L1 (harvested after 10 days of differentiation induced by the insulin (5 µg/ml) and indomethacin (125 µM) combination) are stimulated with substance C at 1% (v/v) for 24 hours. The culture supernatant is then removed and its IL-6 content measured by ELISA (Enzyme Linked Immunosorbent Assay) according to the supplier's instructions (R&D Systems, Abingdon, GB). The quantity of IL-6 secreted is compared with that of a control culture treated only with the solvent for substance C (ethanol/water (50/50) mixture, diluted 1/100 in the culture medium) and of a culture stimulated with a reference IL-6 inducer, TNF-α at 50 ng/ml (Fried S.K. J. Clin. Endocrinol. Metab. 1998, 83, 847-860). Figure 1 shows that substance C stimulates the production of IL-6 from the adipocytes 3T3-L1 by a factor of about 5 compared with the solvent control culture (43 pg/ml against 9 pg/ml respectively), that is 83% of the effect obtained with the reference inducer (52 pg/ml).

The results obtained show that, on the one hand, substance C recognizes the adipocytes as induction target and that, on the other hand, under the effect of substance C, the basal production of IL-6 by the adipocytes is increased by a factor of 5, that is 83% of the maximum effect obtained with the positive control.

Such an increase makes it possible, taking into account the known properties of IL-6, to envisage, in a first instance, a reduction of the synthesis of the enzyme charged with the entry of the fatty acids, LPL, and then following that, a reduction in the entry of the fatty acids.

## **2- Effect of substance C on adipocyte differentiation**

The objective of this second study was to identify the effects of substance C on the formation of new adipocytes.

The influence of substance C on the differentiation of the preadipocytes 3T3-L1 into mature adipocytes is studied, on the one hand, by evaluating the synthesis of the hormone leptin, a marker of adipocyte differentiation, and, on the other hand, by observing under the microscope the formation of intracytoplasmic lipid vesicles, other indicators of the functional transformation into mature adipocytes. In all cases, substance C is introduced into the culture at 1% (v/v) at the beginning of the differentiation process (induced as above) and

maintained up to its end. The synthesis of leptin is evaluated every two days by ELISA assay (R&D Systems, Abingdon, GB).

Figure 2 shows that in the presence of substance C, the production of leptin remains at an extremely low level throughout the 10 days of the experiment and is markedly lower ( $\leq 200$  pg/ml) than that observed in the control culture which, as expected, sees its leptin level increase from the 2nd day following the induction of differentiation, and increases up to a maximum plateau of 1200-1400 pg/ml from the 6th day. The inhibition of the synthesis of leptin by substance C constitutes the first parameter for the blocking of the adipocyte differentiation process.

The second is provided by the experiment shown in Figure 3 which indicates that after 10 days of differentiation, the control cells develop a morphology of mature adipocytes containing large lipid vesicles which occupy practically the entire cytoplasmic space (A), whereas the same cells treated with substance C remain at a very immature stage with a few rare vesicles which are much smaller in size (B).

Using the 3T3-L1 model, commonly used in the literature for the exploration of adipocyte functions, it has been demonstrated that substance C has the dual property of stimulating, in mature adipocytes, the production of IL-6 and of inhibiting, in precursor

cells, the transformation into mature adipocytes.  
Substance C therefore acts upstream by preventing  
adipocyte maturation and downstream by stimulating, at  
the level of the mature adipocytes, the production of a  
5 cytokine which is involved in limiting the storage of  
fatty acids.

These results support the unique property of  
the substance to induce the production of IL-6 by the  
adipocytes whose autocrine function (on the producing  
10 cells) and paracrine function (on the cells in the  
vicinity of the producing cells) is exerted both on the  
entry of fatty acids into the mature adipocytes, and on  
the recruitment of new adipocytes, by a termination of  
the differentiation of the preadipocytes.

15 Preliminary clinical studies have been  
carried out with slimming compositions according to the  
invention which contain the 3 active substances  
(hereinafter called composition Am2).

Two clinical studies were carried out with  
20 composition Am2.

The first relates to the measurement of the  
thickness of the subcutaneous adipose tissue, and the  
second uses the centimetric measurement.

1) Measurement of the thickness of the  
25 subcutaneous adipose tissue

The objective of this study is to evaluate  
the clinical efficacy of the novel composition Am2  
containing the 3 active substances.

The protocol used is described below.

Number of subjects: 61 healthy female  
volunteers, divided into 2 groups (31 subjects using  
the slimming composition Am2 containing the 3 active  
5 substances, 30 subjects the slimming composition Am1).

The products are applied twice per day over  
the whole of the thighs by a circular massage which is  
stopped after complete penetration of the product.

The evaluation of the efficacy was determined  
10 over a period of 2 months by measuring the thickness of  
the subcutaneous adipose tissue at  $T_0$ ,  $T_{28}$  days,  $T_{56}$  days.  
The method used is that of echography.

The site for the measurement is identified by  
a skin marking and by the height at which the probe is  
15 positioned.

To facilitate the vertical identification and  
to avoid any movement or compression of the tissues  
during the measurement, the echographic probe is placed  
on a stable device, which can be adjusted in height and  
20 independently of the operator.

Three images are acquired successively at the  
level of the identification mark. On each image, 3  
measurements of thickness are performed. All the 6  
measurements thus obtained make it possible to obtain a  
25 precision of  $\pm 1$  mm.

These measurements are supplemented with  
monitoring of the weight of the subjects included in  
the trial and with an analysis of the self-evaluations.

The significance of the results are evaluated by means of Student's t test for paired groups. The test is applied to the raw values as well as to the variation of these parameters over the duration of the trial (value expressed in terms of  $T_0$ ).

Regardless of the group considered, the average weight remained stable during the entire duration of the study and is not therefore likely to be responsible for the variation in the measurement of the thickness of the subcutaneous adipose tissue of the thighs.

The study conditions selected do not make it possible to confirm a significant slimming effect for composition Am1: after 1 month of application, a reduction of 0.8% of the subcutaneous adipose tissue is observed and at 2 months a reduction of 2.6% is observed.

Composition Am2 makes it possible to obtain a very significant slimming effect from the 28th day of application ( $p < 10^{-5}$ ): the reduction in the subcutaneous adipose tissue observed with composition Am2 is -2.2% at 1 month and -4.3% at 2 months of application.

1) Centimetric measurement

The protocol below was used.

Number of subjects: 39 female volunteers divided into 2 groups: 20 received composition Am1 and 19 composition Am2.

The products are applied twice per day for 2 months.

The evaluation of the slimming efficacy was evaluated by centimetry at  $T_0$ ,  $T_{28}$  days and  $T_{56}$  days at the level of the thighs (at 3 cm below the buttock fold), on the right and on the left.

Regardless of the group considered, the average weight is substantially constant during the entire duration of the study and is not therefore likely to be responsible for the variations in the measurement of the thickness of the subcutaneous adipose tissue of the various regions studied.

Table 1 presents the significant results obtained by centimetry.

15

**Table 1:** Results obtained by centimetry

| COMPOSITION     | % of subjects |          | Reduction range |          |
|-----------------|---------------|----------|-----------------|----------|
|                 | 1 month       | 2 months | 1 month         | 2 months |
| Composition Am1 | 30            | 45       | 1-2.0 cm        | 1-2.0 cm |
| Composition Am2 | 72            | 73       | 1-3.5 cm        | 1-2.5 cm |

Composition Am2 has a better slimming activity versus  $T_0$  than composition Am1, from one month of application.

Comparison of the results obtained following these two studies makes it possible to identify the

marked superiority of composition Am2 over its placebo, and also reveals the better performance of composition Am2 compared with composition Am1.

Thus, although sharing part of the mode of  
5 action through substances A + B and their efficacy on lipolysis, the intensity of the beneficial effects obtained with the novel formula Am2 is reinforced by virtue of the action of substance C on the entry of fatty acids into the adipocytes.

10 The combination of these effects, backed by the activity on the recruitment of new adipocytes, makes it possible to reduce the importance of the existing adipose tissue and to prevent its development.

In the preparation of the compositions  
15 according to the present invention, the extracts thus constituted are mixed with aqueous or nonaqueous solvents and with conventional diluents which are compatible with a topical use as well as with the active components of the same composition. Appropriate  
20 solvents and/or diluents will be chosen according to their capacity to transport the active component of the extract of the invention into the subcutaneous adipose layer.

These compositions generally contain  
25 excipients or additives chosen from the ingredients usually used in compositions intended for local application depending on the requirement of the particular formulations envisaged.

They may contain, for example, thickening agents, demulcents, emollients, stabilizers, preservatives, antifoaming agents, surfactants, antioxidants, colorants and/or pigments, and perfumes.

5           They may also contain other active components which have either an effect of the same type, for example products which contribute to the regulation of lipolysis/lipogenesis or products useful in this type of topical composition such as stimulators of the  
10 synthesis of collagen, inhibitors of collagenase or of elastase, and vasoprotective agents.

The cosmetic compositions of the present invention contain substances A, B or C in proportions of between 0.00001% and 5% relative to the total weight  
15 of the composition, in the form of a mixture with the excipients commonly used for the preparation of cosmetic formulations to be applied to the skin.

The said proportions may vary in the range indicated above depending on the intrinsic activity of  
20 the components included in the composition. Preferably, components A, B and C are present in proportions of 0.0001% to 2%.

An advantageous form of the compositions according the invention is a fluid which is topically  
25 applied by means of an adhesive support, designated hereinafter "patch", this patch allowing controlled diffusion of the active components.

The compositions of the present invention have good stability and can be preserved for the period necessary for use at temperatures between 0°C and 60°C without there being sedimentation of the constituents  
5 or separation of the phases, or a reduction in activity which can compromise their use.

These compositions are very well tolerated; they exhibit no phototoxicity and their application to the skin, for prolonged periods, involves no side  
10 effect.

From the first applications, the skin relief is smooth, the skin becomes more tonic and firm. After applying for one month, the slimming effect appears, the "orange skin" appearance visibly diminishes and the  
15 figure becomes slimmer.

**EXAMPLE 1**

Slimming composition in the form of a spray patch

| Raw materials                                                                                | Quantity % by weight |
|----------------------------------------------------------------------------------------------|----------------------|
| Demineralized water                                                                          | qs 100               |
| Covacryl AC (sodium polyacrylate)                                                            | 0.8                  |
| Covacryl RM (sodium polyacrylate)                                                            | 1.4                  |
| PVP K30 (PVP)                                                                                | 0.2                  |
| Covacryl A15 (acrylate copolymers)                                                           | 7                    |
| Covacryl E14 (acrylate copolymers)                                                           | 3                    |
| Covaplast (acetyltributyl<br>citrate/triethyl citrate/trioctyl<br>trimellitate/ethyl lactate | 2.5                  |
| Simusol 98 (Oleth-20)                                                                        | 0.5                  |
| Dermosoft octiol (ethylhexanediol)                                                           | 0.5                  |
| Substance A                                                                                  | 0.14                 |
| Substance B                                                                                  | 0.007                |
| Substance C                                                                                  | 0.5                  |
| Propellant gas (butane)                                                                      |                      |

**EXAMPLE 2**

Slimming composition in the form of a spray patch

| Raw materials                                                                             | Quantity % by weight |
|-------------------------------------------------------------------------------------------|----------------------|
| Demineralized water                                                                       | qs 100               |
| CMC 7 LF (cellulose gum)                                                                  | 0.5                  |
| Natrosol 250 HX<br>(hydroxethylcellulose)                                                 | 0.3                  |
| Aquatrix part B (water and<br>carboxymethylchitosan and paraben)                          | 13                   |
| Demineralized water                                                                       | 20                   |
| Aquatrix part A (demineralized water<br>and PVP)                                          | 13                   |
| Phenonip (phenoxyethanol,<br>methylparaben, propylparaben,<br>butylparaben, ethylparaben) | 1                    |
| Simulsol 98 (Oleth-20)                                                                    | 1                    |
| Substance A                                                                               | 0.08                 |
| Substance B                                                                               | 0.004                |
| Substance C                                                                               | 0.25                 |
| Propellant gas (butane)                                                                   |                      |

**EXAMPLE 3**

Slimming composition in the form of a gel

| Raw materials                                                                             | Quantity % by weight |
|-------------------------------------------------------------------------------------------|----------------------|
| Demineralized water                                                                       | qs 100               |
| Trilon B (tetrasodium EDTA)                                                               | 0.2                  |
| Carbopol 2980 (carbomer)                                                                  | 0.5                  |
| Glycerin                                                                                  | 3.0                  |
| Demineralized water                                                                       | 20                   |
| Lubragel MS (polyglyceryl<br>metacrylate and propylene glycol)                            | 5.0                  |
| Dipropylene glycol                                                                        | 3.0                  |
| Butylene glycol                                                                           | 5.0                  |
| Phenonip (phenoxyethanol,<br>methylparaben, propylparaben,<br>butylparaben, ethylparaben) | 0.65                 |
| Triethanolamine                                                                           | 0.5                  |
| Substance A                                                                               | 0.10                 |
| Substance B                                                                               | 0.01                 |
| Substance C                                                                               | 0.1                  |

**EXAMPLE 4**

Slimming composition in the form of an emulsion

| Raw materials                                                                       | Quantity % by weight |
|-------------------------------------------------------------------------------------|----------------------|
| Demineralized water                                                                 | qs 100               |
| Triethanolamine                                                                     | 0.85                 |
| Lanette 16 (cetyl alcohol)                                                          | 0.5                  |
| Miglyol 812 (caprylic/capric triglyceride)                                          | 2.5                  |
| Stearine TP (stearic acid)                                                          | 1.5                  |
| Super Hartolan (lanolin alcohol)                                                    | 0.2                  |
| Silicon DC 200 fluid (dimethicone or simethicone SI RAL)                            | 0.5                  |
| Generol 122N (soyabean glycine)                                                     | 1.0                  |
| Tegin (glyceryl stearate SE)                                                        | 1.0                  |
| Myglyol 840 (propylene glycol dicaprylate/edicaprate)                               | 7.0                  |
| Eutanol G (alcohol)                                                                 | 1.5                  |
| Montane 60 (Sorbitan stearate)                                                      | 0.43                 |
| Montanox 60DF (Polysorbate 60)                                                      | 0.57                 |
| Carbopol 981 2% solution (carbomer)                                                 | 13.0                 |
| Butylene glycol                                                                     | 6.0                  |
| Phenonip (phenoxyethanol, methylparaben, propylparaben, butylparaben, ethylparaben) | 1.0                  |

|                                                          |       |
|----------------------------------------------------------|-------|
| DL- $\alpha$ -tocopherol acetate (tocopheryl<br>acetate) | 0.1   |
| Substance A                                              | 0.02  |
| Substance B                                              | 0.001 |
| Substance C                                              | 0.3   |

**EXAMPLE 5**

Slimming composition in the form of an emulsion gel

| Raw materials                                                                             | Quantity % by weight |
|-------------------------------------------------------------------------------------------|----------------------|
| Water                                                                                     | qs 100               |
| Trilon B (tetrasodium EDTA)                                                               | 0.03                 |
| Natrosol 250 HX<br>(hydroxyethylcellulose)                                                | 0.25                 |
| Pemulen TR-1 (acrylate copolymer)                                                         | 0.20                 |
| Butylene glycol 1.3 pure                                                                  | 5                    |
| Dipropylene glycol                                                                        | 3                    |
| Triethanolamine                                                                           | 0.2                  |
| Phenonip (phenoxyethanol,<br>methylparaben, propylparaben,<br>butylparaben, ethylparaben) | 1                    |
| DC 2502 (cetyldimethicone)                                                                | 4                    |
| Dermol 105 (isodecyl neopentanoate)                                                       | 3                    |
| Sodium hyaluronate                                                                        | 0.01                 |
| Veragel liquid 1:1 (Aloe barbadensis<br>gel)                                              | 1                    |
| Substance A                                                                               | 0.15                 |
| Substance B                                                                               | 0.1                  |
| Substance C                                                                               | 0.05                 |

**CLAIMS**

1. Slimming cosmetic composition containing  
at least one component inducing the production of IL-6  
5 by the adipocytes in the form of a mixture with an  
excipient for cosmetic preparations.

2. Composition according to Claim 1,  
characterized in that the component inducing the  
production of IL-6 by the adipocytes is chosen from a  
10 nonpeptide synthetic compound, a peptide, a cell or  
tissue extract of animal or plant origin and a product  
obtained from fermentation by a microorganism.

3. Composition according to Claim 2,  
characterized in that the component inducing the  
15 production of IL-6 by the adipocytes is a product  
obtained from fermentation by a microorganism chosen  
from bacteria and fungi.

4. Composition according to Claim 3,  
characterized in that the component inducing the  
20 production of IL-6 by the adipocytes is capable of  
being obtained by fermentation by a *Rhodotorula sp.*  
strain.

5. Composition according to Claim 4,  
characterized in that the component inducing the  
25 production of IL-6 by the adipocytes is capable of  
being obtained by fermentation by the *Rhodotorula sp*  
strain deposited at the C.N.C.M. of Institut Pasteur  
under the number I 1844, or of its producing mutants.

6. Composition according to one of Claims 1 to 5, characterized in that it also contains an  $\alpha_2$  antagonist and NPY antagonist component.

7. Composition according to Claim 6,  
5 characterized in that the said  $\alpha_2$  antagonist or NPY antagonist components are chosen from nonpeptide synthetic products, extracts of cells of tissues of animal or plant origin and products obtained from fermentation by microorganisms.

10 8. Composition according to Claim 7, characterized in that the  $\alpha_2$  antagonist or NPY antagonist components are capable of being obtained by fermentation by microorganisms chosen from bacteria and fungi.

15 9. Composition according to Claim 8, characterized in that the  $\alpha_2$  antagonist component is capable of being obtained by fermentation by the *Bacillus licheniformis* strain deposited at the C.N.C.M. of Institut Pasteur under the number I 1778, or one of  
20 its producing mutants.

10. Composition according to Claim 8, characterized in that the NPY antagonist component is capable of being obtained by fermentation by the *Streptomyces* sp. strain deposited at the C.N.C.M. of  
25 Institut Pasteur under the number I 1132, or one of its producing mutants.

11. Slimming cosmetic composition for topical application containing an NPY antagonist, an  $\alpha_2$

antagonist and an inducer of the production of IL-6 by the adipocytes in combination with a cosmetically acceptable excipient.

12. Composition according to Claim 11,  
5 characterized in that the NPY antagonist, the  $\alpha_2$  antagonist and the inducer of the production of IL-6 are obtained respectively by fermentation by the I 1132, I 1778 and I 1844 strains deposited respectively at the C.N.C.M. of Institut Pasteur.
- 10 13. Use of a slimming composition according to Claim 12 for the regulation of lipolysis/lipogenesis in the skin.