Lipout™
Burns stored fat and achieves centimetric reduction.
RESHAPE YOUR SILHOUETTE

The factors that commonly cause our bodies to accumulate excess fatty tissue include a sedentary life, an unbalanced diet and stress. This excess body fat is of great concern to a majority of the population, for men and women alike of all ages alike. Above all, it is a concern when the time arrives for us to put on our swimsuits and we realize that this unsightly fat will not readily disappear.

Fatty tissue has traditionally been considered to be involved in the absorption of the free fatty acids and triglycerides that circulate in the blood due to an excessive intake of calories. It has long been thought that it then stores them as a passive energy reserve. However, it has now been established that fatty tissue plays an active role in the regulation of metabolism, in homeostasis and in shaping the surface of our bodies.

Subcutaneous fat is also a source of cellulite, cosmetic condition that affects more than 85% of women over 20 years of age (Kruglikov, 2012) and that must be controlled if one wants an attractive figure.

The idea of getting rid of excess fat for a healthy, balanced body is consequently not new; in fact, year after year there is a strong demand for products and procedures that will reduce excess fat.

_Lipout™_ is a cosmetic ingredient that activates the fat-burning mechanisms of adipose tissue to reduce excess fat and remodel your figure.
ADIPOSE TISSUE AND ADIPOCYTES

Subcutaneous adipose tissue is predominantly formed of adipocytes that accumulate lipids in their cytoplasm.

Until recently, it was thought that there were only two types of adipocytes, white and brown; however, recent studies have demonstrated that the human body contains a third type: beige adipocytes.

These three types of adipocytes originate from different precursors (Figure 1). The brown ones share a common origin with skeletal muscle, while white and beige adipocytes come from the same line, although this divides to give two different precursor populations (Rosen & Spiegelman, 2014). This means that each precursor gives rise to a distinct cell line that cannot differentiate to another type of adipocyte (for example, white preadipocytes cannot differentiate to brown adipocytes).

Figure 1. Differentiation of the three types of adipocytes: brown, white and beige.
1. WHITE ADIPOCYTES

White adipocytes are the most well-known type of adipocyte; they give rise to white adipose tissue (WAT) and are our body’s main fat reserve. They are found around the internal organs and beneath the skin.

These adipocytes are large cells that contain few mitochondria, and they store lipids as triglycerides in a single droplet (unilocular).

2. BROWN ADIPOCYTES

Brown adipose tissue is made up of brown adipocytes. These adipocytes are multilocular cells that store lipids in small triglyceride-containing vesicles evenly distributed throughout the cytoplasm; they have a large number of mitochondria that give this tissue a brownish color.

Brown adipocytes specialize in burning fat to produce heat (thermogenesis). They have a high level of thermogenic gene expression, including the most characteristic one, the uncoupling protein 1 (UCP1) gene and the β3-adrenergic receptor (ADRB3) gene. These adipocytes are highly metabolically active and they burn lipids as a fuel in thermogenesis, although they can also use glucose (Wu et al., 2013).

In children, these adipocyte depots are located in specific parts of the body, such as in collarbones and the neck (Cannon et al., 2012), but to date they have never been found in subcutaneous adipose tissue (Cypess, et al., 2009; Van Marken et al., 2009).

3. BEIGE ADIPOCYTES

Recent studies have defined a third type of adipocyte in humans: beige adipocytes. They are bifunctional cells, which means that they can have both active and inactive forms. They possess a gene expression pattern that is different from that of white or brown adipocytes.
When they are inactive their morphology is very similar to that of white adipocytes (unilocular, with few mitochondria) and they have a low basal level of UCP1 gene expression and normal cell respiration. However, with suitable stimulus they undergo a “browning” process (becoming multilocular, with an elevated number of mitochondria). This means that they become metabolically active, the expression of UCP1 increases dramatically and thermogenesis is activated, thereby increasing the burning of fatty acids to sustain increased respiration (Figure 5). When the stimulus disappears the active beige adipocytes once again adopt the morphology and gene expression of white adipocytes and they become inactive. This transformation from inactive to active can be repeated with the right stimulation (Rosenwald et al., 2013).

A number of endogenous inductors of this browning have been discovered and they all have their own receptors on the adipocyte cell membrane (Harms & Seale, 2013). For instance, the β3-adrenergic receptor becomes activated in response to the cold, amongst other stimuli, and it is an important regulator of the thermogenesis process in brown and beige adipocytes.

Recent studies have shown that beige adipocytes develop from beige preadipocytes (Wang et al., 2013). However, some studies suggest that it may be also possible for them to develop from mature white adipocytes (Vitali et al., 2012).

The latest research has shown that beige adipocytes replace the brown ones in adults (Wu et al., 2012). It has also been found that under certain conditions beige adipocytes can also be present in subcutaneous depots of white adipocytes (Wu et al., 2012; Wu et al., 2013; Rosen & Spiegelman, 2014). Studies carried out on adults have demonstrated that the activity of these beige adipocyte depots can be increased by applying various exogenous factors such as cold or by the ingestion of certain foods. It has also been observed that the mass and activity of beige adipose tissue decreases as body mass index increases or as

![Figure 4. Active (left) and inactive (right) beige adipocytes.](image)

![Figure 5. Outline of thermogenesis and respiration in brown and beige adipocytes.](image)
we grow older, causing an accumulation of body fat. Therefore, **beige adipose tissue activity is highly important because it contributes to reducing body fat** (Yoneshiro *et al*., 2013).

### THERMOGENESIS: A FAT-BURNING PROCESS

**Thermogenesis** is the process by which an organism produces thermal energy or heat. This process takes place in parallel with cellular respiration and is initiated in brown or beige adipocytes through the stimulation of surface receptors.

Triglyceride degradation is initially activated and intracellular fatty acids are liberated. The great majority of these acids enter the mitochondria to fuel cellular respiration (β-oxidation, Krebs cycle).

A small portion of these free fatty acids activate **UCP1**, a protein found on the inner mitochondrial membrane of brown and beige adipocytes. This is the **essential element for thermogenesis**, in addition to being the marker gene of these adipocytes. It catalyzes the flow of protons across this membrane in parallel with the respiratory chain, thereby dissipating the electrochemical gradient generated by the respiratory chain.

Fatty acids are essential for the activation and functioning of UCP1 but UCP1 does not oxidize them. They are, in fact, oxidized in the β-oxidation cycle in order to fuel cellular respiration. In cells that lack UCP1, the proton gradient can only be dissipated through ATP formation; that is, the protons pass through a number of complexes in the respiratory chain before reaching ATP synthase, thereby supplying the energy necessary to produce ATP. However, when high levels of ATP are present in the cell, the transport of protons through ATP synthase decreases and the oxidation of fatty acids halts. The presence of activated UCP1 therefore allows the acceleration of cellular respiration even when there is an elevated level of ATP in the cell, generating ATP (respiration) and heat (thermogenesis) (Wu *et al*., 2013).

This means that **increasing UCP1 expression alone is insufficient to burn fat. Its activation, together with the subsequent stimulation of mitochondrial fatty acid oxidation, is also necessary to activate thermogenesis** (Ouellet *et al*., 2012) and as a consequence **increase cellular respiration. This results in a greater consumption of lipids** – that is, the induction of a fat-burning effect.
Lipout™ is an alternative to invasive treatments for reducing accumulated body fat thanks to its ability to transform fat-accumulating adipose tissue into tissue that actively burns fat.

Lipout™ contains an extract of *Tisochrysis lutea* (previously *Isochrysis galbana*), a unicellular algae with a standardized xanthophylls concentration that is rich in polyunsaturated fatty acids and which induces the formation of active beige adipocytes. Lipout™ simultaneously activates the following mechanisms:
1. **Induction of UCP1** expression in white and inactive beige adipocytes in order to induce their browning; that is, convert them into active beige adipocytes.

2. **Increase in β-oxidation of fatty acids** thanks to the activation of thermogenesis, literally burning the fat accumulated in the beige and white adipocytes.

The activation of both mechanisms allows effective burning of fat through thermogenesis, thanks to the browning of subcutaneous adipose tissue.

*Lipout™* activates browning and thermogenesis processes in adipocytes, burning fat to refine and reshape your silhouette

**COMPOSITION**

*Tisochrysis lutea* is a unicellular microalga belonging to the group *Haptophyta*. It contains approximately 37% proteins and a high percentage of fatty acids (up to 47% polyunsaturated fatty acids or PUFA) (Sánchez *et al.*, 2000; Gouveia *et al.*, 2008).

*Tisochrysis lutea* also contains pigments (Zapata & Garrido 1997; Obata & Taguchi 2012):

- Chlorophyll *a* and *c*.
- Xanthophylls such as fucoxanthin, diatoxanthin and diadinoxanthin.

*Lipout™* is obtained through a biotechnological process from *Tisochrysis lutea* and therefore constitutes a renewable source of active ingredient. Cultivating the microalgae in closed photobioreactors allows us to obtain a high quality product with optimized levels of metabolites and pigments under reproducible and controlled conditions. In addition, pollutant contamination is eliminated and the environmental impact is notably reduced.
IN VITRO EFFICACY

IN VITRO STUDY PROTOCOL

Since there is still no consensus whether beige adipocytes can only develop from beige preadipocytes or they can also interconvert from white adipocytes, the in vitro study simulated both possible scenarios:

- We used cultures of preadipocytes from human subcutaneous adipose tissue, in order to evaluate Lipout™'s potential for inducing the differentiation of beige preadipocytes to mature and active beige adipocytes. The preadipocytes were incubated with Lipout™ for the first 7 days of development, followed by 7 days incubation in a standard differentiator medium until their complete maturation.

- We also evaluated Lipout™'s capacity to convert inactive beige adipocytes into active ones and/or interconvert mature white adipocytes into active beige adipocytes. In order to do this we treated a culture of human subcutaneous a priori white mature adipocytes with Lipout™ for 2 weeks. The cells used were isolated from the subcutaneous tissue of volunteers.

To demonstrate that Lipout™ activates beige adipocytes and thermogenesis, we performed our in vitro study in four steps, evaluating:

1. Expression of key genes in the thermogenesis process.
2. Expression of thermogenic proteins, to confirm the previous step.
4. Quantification of β-oxidation, to confirm the functionality of the induced changes.

1. EXPRESSION OF KEY GENES IN THE THERMOGENESIS PROCESS

The first step of the study was to evaluate whether Lipout™ is capable of inducing the expression of the key thermogenisis marker UCP1 both in cultures of subcutaneous preadipocytes as well as in cultures of a priori mature white adipocytes. This step was performed using polymerase chain reaction (PCR).

We observed a dramatic increase in the expression of the UCP1 gene in both types of culture, which was most marked at the highest Lipout™ concentrations. Gene expression increased by 2,094% in preadipocyte cultures (Graph 1) and by 537% in the mature adipocyte culture at the highest Lipout™ concentration (0.56%), compared to the control (Graph 2).
These extremely high values for gene expression were seen because the level of UCP1 gene expression in the control culture was near zero.

Graphs 1 and 2. Variation in the relative quantity of UCP1 mRNA observed at the end of the preadipocyte incubations (left) and of the mature adipocytes incubations (right) with Lipout™, compared to the control.

These results indicate that Lipout™ activates the genetic program of the beige adipocytes in the white adipose tissue.

2. EXPRESSION OF KEY PROTEINS IN THE THERMOGENESIS PROCESS

After the positive gene expression results, we assessed whether Lipout™ actually activates the expression of the UCP1 protein. An evaluation was carried out using immunocytochemistry. We also evaluated the expression of the voltage-dependent anion channel (VDAC) protein, which is an indicator of biogenesis of new mitochondria in cells.

It was observed that the expression of both proteins increased, by 50% in preadipocytes and by 378% in mature adipocytes with an increase of Lipout™ concentrations. The same pattern was observed for VDAC, whose expression increased by 22% in preadipocytes and by 139% in mature adipocytes.

The increase in UCP1 expression after incubation with Lipout™ is clearly visible on the microscope images of the treated adipocyte cultures (Figures 10 and 11), compared with untreated cultures (Figures 8 and 9).

These results indicate that the gene expression induced by Lipout™ translates into an increase in the production of proteins essential for thermogenesis.
3. BIOGENESIS OF NEW MITOCHONDRIA

Mitochondria are the most important organelles in the processes of respiration and thermogenesis. By using a specific marker we were able to demonstrate that the increase in the expression of the VDAC protein caused by Lipout™, as measured in the previous assay, resulted in a significant increase in the number of active mitochondria in the cells (Figures 14 and 15).

Figures 8-11. Microscope images of UCP1 expression in preadipocyte cultures (left) and mature adipocytes (right), without treatment (upper) and treated with Lipout™ (lower) (UCP1 is clearly visible as yellowish-red stains).
Figures 12-15. Microscope images of active mitochondria in the subcutaneous preadipocyte cultures (left) and mature adipocytes (right) without treatment (upper) and treated with Lipout™ (lower). The active mitochondria are stained with a specific marker, MitoTracker Red. The blue stains visible in the upper panel are cell nuclei. The active mitochondria are visible in the lower panel as bright yellow stains.

4. INCREASE IN FATTY ACID OXIDATION

The final step of our in vitro study was therefore to assess whether the incubation of adipocytes with Lipout™ increased the oxidation of fatty acids.

Treatment with the highest concentration of Lipout™ increased β-oxidation by 118% in preadipocytes (Graph 3) and 173% in mature adipocytes (Graph 4).

These results show that the activation of the genetic program and of protein production by Lipout™ is followed by an increased elimination of lipids stored in white and beige adipocytes.
3. β-oxidation in preadipocytes

4. β-oxidation in mature adipocytes

Graphs 3 and 4. Increase in fatty acid oxidation in a priori white preadipocytes (left) and a priori white mature adipocytes (right) treated with Lipout™, compared with the control. CCPM = corrected counts per minute.

**IN VIVO EFFICACY**

*Lipout™*’s efficacy in reducing body fat and cellulite was evaluated in an *in vivo* double-blind study with the following parameters:

- 61 volunteers, men and women, between 18 and 60 years of age, all with a body mass index (BMI) of above 23 for the women and above 25 for the men.
- A cream-gel with 3% *Lipout™* was compared with the same formulation without active ingredient (placebo).
- 21 women and 10 men applied the placebo and 20 women and 10 men applied the formulation with *Lipout™* twice a day for 2 months.
- Women applied the product on their abdomen, hips and thighs in order to evaluate fat and cellulite reduction. Men applied the product on their abdomen only in order to evaluate fat reduction.
- The volunteers did not apply any other product or treatment during the study. They were instructed not to change diet or life-style habits during the study.
- The following parameters were evaluated at the start (D0), after a month of treatment (D28) and at the end of the study (D56):
  1. Reduction in fat layer:
Measurements of body perimeter in centimeters.
Standardized photos of the treated body areas.
Thickness of the subcutaneous fat layer.

2. Reduction in cellulite:
   - Reduction in the length of the dermis-hypodermis junction.
   - Roughness of the skin.
   - Clinical evaluation.

3. Improvements in the biomechanical properties of the skin:
   - Cutaneous elasticity.
   - Skin firmness.

4. Activation of thermogenesis in the subcutaneous adipose tissue (D0 and D56).

5. Subjective evaluation of the product’s efficacy.

1. REDUCTION IN FAT LAYER

Measurements of body perimeter in centimeters

A flexible tape measure was used to measure the female volunteers’ hips and thighs, along with the abdomens of both men and women.

The application of Lipout™ reduced the size of all evaluated areas when compared with the placebo (Graphs 5-8):

- **Thighs:** average reduction of **1.0 cm** at D28 and of **1.4 cm** at D56 of the treatment (Graph 5), with a maximum reduction of **5.7 cm**.
- **Hips:** average reduction of **0.7 cm** at D28 and of **1.3 cm** at D56 of the treatment (Graph 6), with a maximum reduction of **5.5 cm**.
• Abdomen:
  o **Women:** average reduction of **1.4 cm** at D28 and of **2.2 cm** at D56 of the treatment (Graph 7), with a maximum reduction of **5.0 cm**.
  o **Men:** average reduction of **1.2 cm** at D28 and of **1.7 cm** at D56 of the treatment (Graph 8), with a maximum reduction of **10.4 cm**.

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Graphs 5-8. Average values for reductions in centimeters in the outline of the thighs, hips and abdomen, obtained after 1 month (D28) and 2 months (D56) of treatment with Lipout™ and placebo. The centimetric differences obtained by Lipout™ versus the placebo are also shown, within the violet circles. The majority of differences are statistically significant (*P<0.05*).
Standardized photos of the treated body areas

Standardized photographs were taken of the volunteers’ thighs and hips (women) and abdomen (women and men) in order to observe the effect of both trial formulations on these different body areas.

The loss in body volume is visible in the photographs for both men and women (Figures 16 and 17), in addition to an overall improvement in the appearance of the skin (Figure 18).

Figure 16: Standardized photographs of the abdominal area of a male volunteer, showing the reduction in subcutaneous fat tissue at 1 month (D28) and 2 months (D56) of treatment with Lipout™.

Figure 17: Standardized photographs of the abdominal area of a female volunteer, showing the reduction in subcutaneous fat tissue after 1 month (D28) and 2 months (D56) of treatment with Lipout™.

Figure 18: Standardized photographs of the thighs and hips of a female volunteer, where it is possible to see both the reduction in subcutaneous fatty tissue and the improvement in the appearance of the skin after 1 month (D28) and 2 months (D56) of treatment with Lipout™.
Thickness of the subcutaneous fat layer

Subcutaneous fat causes undesired changes in the shape of our figures. Our study evaluated this subcutaneous adipose tissue using ultrasonic measurements (Dermascan C ultrasound system), as shown in Figure 19:

The thickness of the subcutaneous fat was significantly reduced in all areas for the group treated with Lipout™ when compared with the placebo:

- **Thighs:** 13.6% decrease at D28 and 25.5% (0.8 mm) decrease at D56.
- **Hips:** 30.9% decrease at D28 and 49.9% (1.0 mm) decrease at D56.
- **Abdomen:**
  - Women: 13.1% decrease at D28 and 29.3% (1.5 mm) decrease at D56.
  - Men: 52.0% decrease at D28 and 66.5% (1.4 mm) decrease at D56.

_Lipout™ significantly reduces body circumference in both men and women by decreasing the thickness of subcutaneous adipose tissue._
2. REDUCTION OF CELLULITE

Reduction in the length of the dermis-hypodermis junction

Measurement of the dermis-hypodermis junction is one of the standard parameters used to assess the severity of cellulite, as the disorganization of this junction is one of the factors conditioning the formation of cellulite. It is also the factor that causes the orange peel appearance in the skin. It is evaluated by calculating the length of the line that separates the dermis from the hypodermis; the longer this line is, the more severe the cellulite (Figure 20).

Lipout™ significantly reduced the length of the dermis-hypodermis junction (21.7%) compared with the placebo.

Skin roughness

Skin roughness is one of the main symptoms of cellulite and it can be evaluated using fringe projection (PRIMOS 3D). Two parameters were evaluated in the study to assess the roughness of the female buttocks area, which is the area most affected by cellulite:

- **Sa** represents the arithmetic average of the depth of the peaks and troughs present on the surface of the skin.
- **Sz** represents the average of the 5 largest peaks and the 5 deepest troughs in the skin area being evaluated.

Figure 20. Schematic representation of the relationship between the increased length of the dermis-hypodermis junction and the severity of the cellulite.
The application of Lipout™ decreased roughness, expressed as Sa, by 5.7% after one month of treatment and by 10.7% after two months, with a significant difference compared to the placebo (Graph 9).

The application of Lipout™ decreased roughness, expressed as Sz, by 1.9% after one month of treatment and by 13.9% after two months, with a significant difference compared to the placebo (Graph 10).

The following are 3D images obtained using the PRIMOS 3D system; it can be seen that the skin is clearly smoother by D56:
Clinical evaluation

At each of the experimental stages a dermatologist evaluated the cellulite severity using two different clinical grading methods: the Nürnberger-Müller Severity Scale and the Cellulite Severity Scale (CSS). Both are used to evaluate the severity of cellulite taking into account all the characteristics typical of cellulitic skin, such as the number of visible depressions and their depth, as well as the skin’s morphological aspect and degree of flaccidity and laxity.

The clinical evaluation confirmed the results obtained previously, which showed that Lipout™ reduces cellulite:

<table>
<thead>
<tr>
<th>Cellulite Severity Scale</th>
<th>Nürnberger-Müller Scale</th>
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<tbody>
<tr>
<td>Placebo</td>
<td>-4%</td>
</tr>
<tr>
<td>Lipout™</td>
<td>-19%</td>
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Table 1. Average percentage variations in the values obtained during the clinical evaluation of the volunteers at the end of the study (D56).

Lipout™ significantly reduced cellulite by 19% after two months in both clinical assessments.

3. IMPROVEMENTS IN THE SKIN’S BIOMECHANICAL PROPERTIES

The biomechanical properties of the skin were measured using a Cutometer®. The application of probes of different sizes made it possible to assess both the superficial and deeper skin layers.

Cutaneous elasticity

Skin elasticity is a measure of its ability to return to its original position after applying a negative pressure. Among various parameters obtained by the Cutometer®, R7 is the most accurate to represent the elasticity of the skin.

There was a statistically significant improvement in skin elasticity after 28 days of applying Lipout™. This was found in both the superficial and deeper layers for all the body areas evaluated.
- The elasticity of the upper layer of the skin increased by 12.6% by D28 and 24.8% by D56 with Lipout™ compared to the placebo (Graph 11).
- Lipout™ also increased the elasticity of the skin’s deepest layers, by 10.9% by D28 and 19.3% by D56, with a significant difference compared to the placebo (Graph 12).

Graphs 11 and 12. Variation in cutaneous elasticity in upper and lower skin layers (%), obtained with Lipout™ and the placebo at D28 and D56 (end of the study) versus D0 and versus placebo. (*) Statistically significant difference (P<0.05).
Skin firmness

Firmness relates to the resistance of the skin under negative pressure. This property was measured using the Cutometer® and the parameter F4 (the lower the reading, the greater the skin firmness).

There was a statistically significant decrease in F4 after 28 and 56 days for the skin of the group applying Lipout™, both in superficial and deeper layers (Graph 13 and 14). This means that the skin firmness increased significantly with Lipout™ in comparison with the placebo. Firmness increased by 16.1% in superficial layers and by 11.7% in deeper layers after a month, and by 25.5% in superficial layers and 28.9% in deeper layers after two months of Lipout™ application.

**Graphs 13 and 14. Variation in skin firmness in upper and lower skin layers (%), obtained with Lipout™ and the placebo at D28 and D56 (end of the study) versus D0 and placebo. (*) Statistically significant difference (P<0.05).**

* Lipout™ improves the condition of the skin, softening the cellulite appearance
4. ACTIVATION OF THERMOGENESIS IN SUBCUTANEOUS ADIPOSE TISSUE

Given that Lipout™ activates the essential mechanisms that promote thermogenesis in fatty tissue, an evaluation was made as to whether applying Lipout™ resulted in an increase in skin temperature, reflecting this fat-burning activity. Skin temperature in the treated areas was evaluated at D0 and D56 using thermography images of the relevant body areas: the abdomen in men and women and the hips and thighs for women.

Figure 22. Thermographic images obtained before (D0) and after 2 months (D56) of treatment with Lipout™. The upper panel shows the abdominal area of a male volunteer, the middle panel shows the back of a female volunteer and the lower panel shows the front of a female volunteer.
Lipout™'s effect on skin temperature is clearly visible on the thermographic images (Figure 22). On the images from the beginning of the study colder areas (violet) can be seen for both men and women. These cold areas indicate the presence of thermogenically inactive tissue (lipid storage). After two months of treatment with Lipout™ the violet areas become orangey-red, indicating a significant increase in fat-burning thermogenic activity. These results confirm that Lipout™ induces thermogenesis in vivo, as well as in vitro as was previously demonstrated.

Lipout™ application significantly increases skin temperature (Graph 15):

- For women, Lipout™ application gave a difference of 0.9°C versus the placebo at D56.
- For men, Lipout™ application gave a difference of 1.3°C versus the placebo at D56.

**Graph 15. Variation in skin temperature obtained by Lipout™ and the placebo after 2 months of treatment.**

* Lipout™ increases skin temperature, indicating an increase in thermogenic activity of subcutaneous fatty tissue
5. SUBJECTIVE EVALUATION OF THE PRODUCT EFFICACY

**Lipout™'s** efficacy was assessed by a self-evaluation questionnaire completed by volunteers both during and at the end of the study (Graph 16).

**16. Subjective evaluation**

<table>
<thead>
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<td>* Elasticity improvement</td>
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</tr>
<tr>
<td>* Cellulite reduction</td>
<td>60%</td>
</tr>
<tr>
<td>* Firmness improvement</td>
<td>40%</td>
</tr>
<tr>
<td>* Global evaluation</td>
<td>20%</td>
</tr>
<tr>
<td>* Purchasing intention</td>
<td>0%</td>
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* Placebo
* Lipout™

Graph 16. Evaluation of the placebo and **Lipout™** by the volunteers, indicating the percentage of volunteers that replied “Agree” and “Completely Agree” to the survey questions. (*) Statistically significant difference between results obtained in groups of **Lipout™** and placebo (P<0.05).
CONCLUSIONS

Lipout™ induces the browning of a priori white adipocytes thanks to the xanthophylls and polyunsaturated fatty acids it contains.

This indicates that Lipout™ induces the differentiation of beige preadipocytes into mature beige adipocytes. It also transforms lipid storing adipose tissue into lipid burning adipose tissue by activating inactive beige adipocytes and converting white adipocytes into beige ones.

By demonstrating an increase in the β-oxidation of fatty acids in treated cultures we confirmed that the beige adipocytes differentiated and activated by Lipout™ actively burn lipids thanks to the activation of thermogenic mechanisms. Lipout™’s capacity to induce thermogenesis was confirmed in vivo by an increase in the skin temperature of volunteers following Lipout™ application.

These results indicate that Lipout™ is an active ingredient capable of bringing about browning of subcutaneous adipocytes and of activating thermogenesis to burn fats in adipose tissue, leading to a reduction in the thickness of subcutaneous fat in both men and women.

Lipout™ significantly reduces fat, increases the skin elasticity and firmness and also acts as an anti-cellulite by reducing various characteristics related to this condition.

COSMETIC APPLICATIONS

- Slimming and body-shaping products.
- Prevention and treatment of cellulite.
- As a complementary ingredient in body-care products.
RECOMMENDED DOSE

The recommended dose is between 1% and 3%.

BIBLIOGRAPHY


