

# LIPO REDUX

PRO FOR



Body slim and shape management

Body contouring with lipolytic action

Improves the appearance  
of all visible signs of cellulite

# CLA CARNITINE

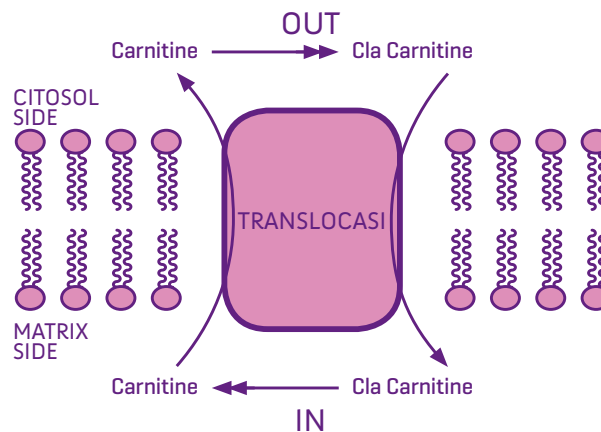
## ANTI-CELLULITE LIPOLYTIC AND TONING SUBSTANCE

### >> CLA CARNITINE

When taking into consideration the structures, the two partners [Carnitine and CLA] and CLA's biological activity, the following can be said:  
> The acid of CLA can be esterified with L-carnitine [in CLA Carnitine the acyclic chain is represented by linoleic acid conjugated with double bonds].

> Both partners of the resulting molecule have a high biological action, therefore the properties of CLA Carnitine can be expected to be superior to those of each single ingredient.

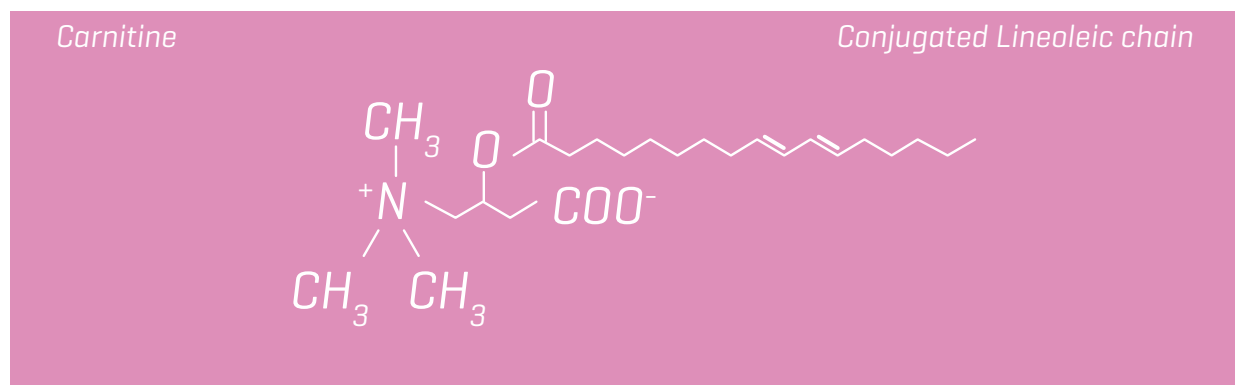
**L-carnitine** makes possible the transport of long-chain fatty acids from cytosol to the mitochondria, where the process continues with the oxidation, Krebs cycle and oxidative phosphorylation, until the production of energy in ATP form.



**CLA** [or conjugated linoleic acid], is a mixture of isometric forms of linoleic acid [a fatty acid with 18 carbon atoms and two double bonds]. Linoleic acid is an essential fat, meaning that it cannot be synthesized as it is by our organism. It is found only in nature. In the digestive system, Linoleic acid is transformed into CLA. Recent research has shown that CLA promotes the reduction of body fat and facilitates thin mass development. The first clinical research of the properties of CLA was conducted in 1997. This double-blind study had a duration of 90 days, and its results showed a 20% decrease in body fat without a significant weight shift. In a study conducted on animals for the purpose of assessing CLA's action dynamic in relation to lipidic metabolism, results showed that **CLA intake reduced the dimension of adipocyte without reducing their number.**

### Chemical structure of CLA Carnitine

Linoleic acid esters bonded with trimethyl L-carnitine amino acid play an important role in the energy production process from lipids resulting in a reduction of body fat.



# 97% FORSKOLIN

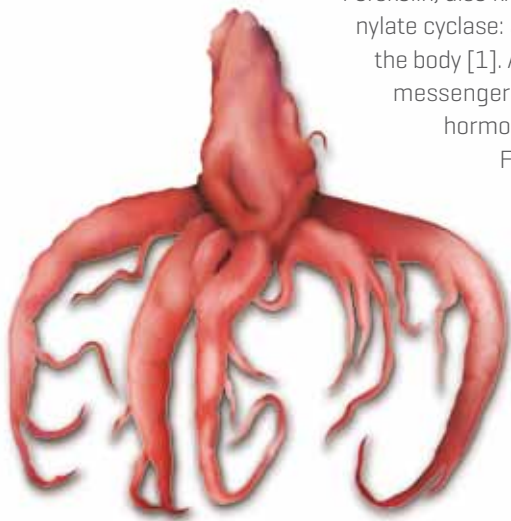
## COLEUS EXTRACT THERMOGENIC AND LIPOLYTIC AGENT

### >> PLANT DESCRIPTION

*Coleus forskohlii* is a perennial member of the Lamiaceae family that was first discovered in the lower elevations of India. Today, it is grown around the world as an ornamental and medicinal plant. The root, which is the only part of the plant to contain the active principle, is used for a myriad of pharmacological purposes. As recorded in ancient Sanskrit texts, Coleus has traditionally been used as a medicinal herb to treat heart and lung diseases, intestinal spasms, insomnia and convulsions. The name of the genus "Coleus" derives from the Greek "Koleos" meaning sheath, from the shape of the stem base. There are more than 300 species in the Coleus genus. *Coleus forskohlii* is an important traditional Ayurvedic herb that has been a key part of Indian medicine for centuries. In the 1970s, researchers isolated a chemically active ingredient in the herb and called it Forskolin. *Coleus forskohlii* extract is produced from the root of *Coleus Forskohlii* with a special extraction process that allows a never reached, maximum purity level of the active principle. It is carefully analyzed and guaranteed to contain not less than 97% Forskolin.



### >> FORSKOLIN EFFECTS



Forskolin, also known as Coleonol or Colforsin, is a labdane diterpene that activates the enzyme adenylate cyclase: a turnkey compound that initiates a cascade of important events within each cell of the body [1]. Adenylate cyclase and the other biochemical molecules it activates include a "second messenger" system that is responsible for carrying out the complex and powerful effects of hormones in the human body.

Forskolin directly activates adenylate cyclase and raises cyclic AMP levels in a variety of tissues. Cyclic AMP is an important cell regulating compound. Once formed, it activates many other enzymes involved in diverse cellular functions [2,3]. Under normal circumstances cAMP is formed when stimulatory hormone [e.g. epinephrine] binds to a receptor site on the cell membrane and stimulates the activation of adenylate cyclase. This enzyme is incorporated into all cellular membranes and only the specificity of the receptor determines which hormone will activate it in a particular cell. Forskolin appears to bypass the need for direct hormonal activation of adenylate cyclase. As a result of this direct activation, intracellular cAMP levels rise. The physiological and biochemical effects involved in this increase include: inhibition of platelet activation; inhibition of mast cell degranulation and histamine release; increased force of contraction of the heart muscle; relaxation of the arteries and other smooth muscles; increased insulin secretion; and increased thyroid function [4]. Studies in humans have shown that direct application of a preparation containing forskolin to the eyes lowers the eye pressure, thereby decreasing the risk of glaucoma [2].

## >> BODY FAT AND BODY SHAPE MANAGEMENT

By facilitating the physiological hormonal action, cyclic AMP may regulate the body's thermogenic response to food, increase the body's metabolic rate and the utilization of body fat, since thermogenesis is preferentially fuelled by fatty acids derived from body fat and/or from food. Since, at least for the moment, there are not enough clinical trials supporting the use of forskolin alone for losing body weight, it is most commonly used as an adjuvant to a weight loss regimen rather than a primary slimming strategy. Studies of acute and chronic toxicity suggest a favorable therapeutic index and confirm the extreme safety of use. For this reason, the employ of Forskolin in body fat and body shape management mainly via "nutraceutical" delivery systems is quickly diffusing, but also the topical application in cosmetic treatments against cellulites and cutaneous fat deposition is continuously expanding [5,6,7].

## >> TANNING AND UV-PROTECTION

The topical application of Forskolin to the skin of fair-skinned melanocortin-1-receptor MCR1-defective mice with epidermal melanocytes resulted in accumulation of eumelanin in the epidermis and was highly protective against UV-mediated cutaneous injury. This study suggests that topical Forskolin treatment can be associated with persistent melanisation, epidermal cell accumulation and increased skin thickening. Another study underlines that the ability of Forskolin to increase intracellular levels of cAMP leads to keratinocytes protection from UVB-induced apoptosis. This takes place independently from the amount of melanin in the skin. Moreover, Forskolin has a protective effect against the cell damage induced by UVB exposure. Indeed, it enhances the removal of the two major types of UVB-induced DNA adducts [cyclobutane-pyrimidine dimers and 6,4-photo-adducts] by facilitating, in this way, the DNA repair. These findings suggest new preventive approaches to photo-aging treatment, by the use of topical formulation containing Forskolin as bioactive agent to increase the body's capacity to repair DNA damages [8,9,10,11].

## >> PHYSICAL AND CHEMICAL CHARACTERISTICS

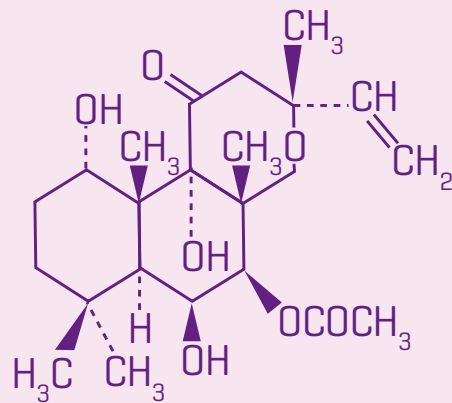
**INCI EU / CTFA:** Coleus Forskohlii Root Extract

**CAS [Forskolin]:** 66575-29-9

**Chemical / IUPAC name:** 3R,4aR,5S,6S,6aS,10S,10aR,10bS]-6,10,10b-trihydroxy-3,4a,7,7,10a-pentamethyl-1-oxo-3-vinyl-dodecahydro-1H-benzo[f]chromen-5-yl acetate

**Chemical formula:** C<sub>22</sub>H<sub>34</sub>O<sub>7</sub>

**Chemical structure:**



## >> SAFETY BY ORAL INTAKE

Forskolin is widely used by oral intake to treat allergies and adverse skin conditions such as eczema and psoriasis, obesity, painful menstrual periods, irritable bowel syndrome [IBS], urinary tract infections [UTI], bladder infections, blood clots, sexual problems in men, trouble sleeping [insomnia] and convulsions.

Healthcare providers sometimes give Forskolin intravenously [by IV] for heart failure. Some people breathe in [inhale] Forskolin powder for asthma. Forskolin drops are used in the eyes to treat glaucoma. Typical dosage is 100 to 300 mg/day of an extract containing 10% to 20% Forskolin. There are no major side effects reported in literature, but the consultation of a physician is recommended before using forskolin-supplements [2].

## >> COSMETIC APPLICATION

In order to identify the cosmetic functionality of Forskolin, the previous data are considered. When topically applied, it is in general an effective cellular metabolism stimulator. When adipocytes are taken into account as a target, the Forskolin employ can be well supported for cosmetic body treatments formulated to reduce cellulites and fat deposition. As for the new findings concerning the ability of Forskolin to increase the capacity of repairing the UV-induced DNA damage and to promote melanisation, its employ in sunscreen products may be helpful with multiple benefits:

- > **Increasing the skin's natural resistance to burning and cell damage under UV light**
- > **Decreasing visible signs of photoaging**
- > **Reactivation of aged skin**
- > **Antioxidant activity against cell membrane attack**
- > **Stimulation of a tanning response**

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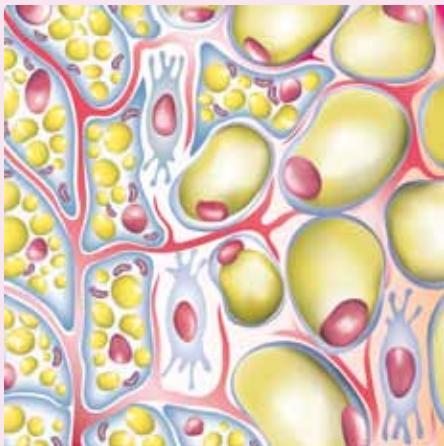
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8. *Passeron T et al. Forskolin Protects Keratinocytes from UVB-induced Apoptosis and Increases DNA Repair Independent of its Effects on Melanogenesis. J Invest Dermatol 2009; 129[1]:162-6;*
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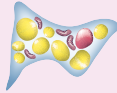
## >> STRUCTURE AND FUNCTIONALITY OF THE ADIPOSE TISSUE

The adipose tissue is composed mainly of two types of cells, the **white adipocytes** and the **brown adipocytes** that have complementary functions, and is heavily vascularized by capillaries.



### WHITE ADIPOCYTES

Store fats or make them available (lipolysis) according to the energy needs. They produce several hormones, amongst which some that directly regulate the metabolism of fats. For example leptin reduces the sensation of hunger.



### BROWN ADIPOCYTES

They burn the fats coming from the white adipocytes producing body heat (thermogenesis).



### CAPILLARIES

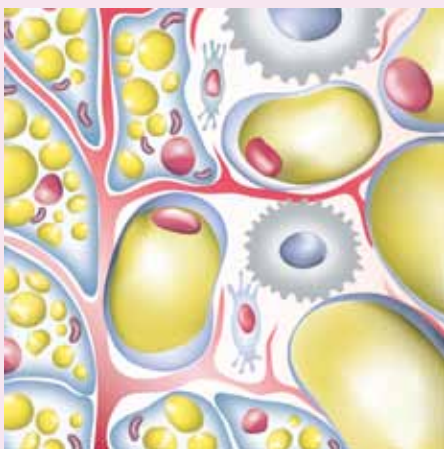
They carry oxygen, essential for burning fat (2 liter of oxygen are needed to burn 1 gram of fat).



### PREADIPOCYTE

Progenitor cell that transforms into white or brown adipocytes, according to necessity.

## >> ALTERATIONS IN CASE OF OVERWEIGHT



In case of an excessive accumulation of fat, the adipose tissue goes through a **progressive increase of free radicals with inflammatory consequences** that modify its functionality.

Thus, the adipose tissue becomes **less reactive** to common weight loss strategies (hypo caloric diet, work outs, lipolitic and thermogenic substances intake)



### MACROPHAGE

They are cells of the immune system recalled in case of an increase in size of the adipocytes and contribute to the inflammatory process.

## >> MECHANISM OF ACTION

Forskolin is a labdane diterpene that activates the enzyme adenylate cyclase: a turnkey compound that initiates a cascade of important events within each cell of the body. Adenylate cyclase and the other biochemical molecules it activates include a "second messenger" system that is responsible for carrying out the complex and powerful effects of hormones in the human body.

By facilitating the physiological hormonal action, cyclic AMP may regulate the body's **thermogenic response**, **increase the body's metabolic** rate and the **utilization of body fat**, since thermogenesis is preferentially fuelled by fatty acids derived from body fat and/or from food.

# LIPOREDUX PRO FOR CLA CARNITINE + FORSKOLIN PURE @97%

NEW ANTI-CELLULITE, LIPOLYTIC, TONING SUBSTANCE.  
THE IDEAL SLIMMING AGENT.

ABLE TO ACT ON LIPIDS (such as triglycerides).

Marketing claim: Thin contour, Lipolytic effect.

## >> EFFICACY TEST

### Materials and methods

The study involved thirty women affected by edematous fibrosclerotic panniculopathy [EFSP] of the thighs according to the following selection criteria:

#### Inclusion criteria:

- > Age: > 18 and < 60;
- > race: caucasian;
- > informed consent form signing;
- > BMI (Body Mass Index): < 30;
- > Blood pressure: SAP/DAP  $\leq$  140/ $\leq$ 90 mmHg; heart rate 50-90 beats per minute [measured in clinostatic position after 5 minutes of rest];
- > Contraceptive methods use for the duration of the study;
- > Motivation and collaboration.

**30 Volunteers** were divided in two groups by random allocation: 15 cases were treated with **Liporedux Pro For** @3% in a cream; the others with placebo.

### Duration of the study

Total duration of the study was **17 weeks** according to the following scheme:

- > Pre-treatment week [run in];
- > First treatment period [four weeks];
- > Wash out [four weeks];
- > Second treatment period [four weeks];
- > Follow up [four weeks];

During treatment periods **Liporedux Pro For** cream was applied every day in the evening on the skin of both thighs in the areas established by the **experimenter**. In the first two days of every treatment period were used 7 ml of product for thigh; in the following twenty six days were used only 5 ml of product for thigh.

**Liporedux Pro For** cream was spread uniformly on unwounded skin then allowed to penetrate with an upwards hand massage [10-15 minutes]. Efficacy and tolerability of the **Liporedux Pro For** cream were evaluated on the basis of parameters [shown in tab. A] recorded during twelve subsequent visits; the "main activity parameter" was **efficacy judgment** expressed by the volunteer as:

**good, sufficient, low, insufficient.**

Experimenters ensured the anonymity of volunteers. On the clinic sheets, data collection folders and other documentation only the experimental code and the first letters of the name appeared.

## >> STUDY DESIGN

| DATA COLLECTION                                      | VISITS                        |                            |                       |                |                 |  |                          |                            |                 |                 |   |                 |
|--|-------------------------------|----------------------------|-----------------------|----------------|-----------------|--|--------------------------|----------------------------|-----------------|-----------------|---|-----------------|
|  | PRE-TREATMENT PERIOD (Run in) | TREATMENT PERIOD 4 weeks   |                       |                |                 | WASHOUT 4 weeks (from T <sub>29</sub> to T <sub>57</sub> ) | TREATMENT PERIOD 4 weeks |                            |                 |                 | FOLLOW UP 4 weeks (from T <sub>85</sub> to T <sub>113</sub> ) |                 |
|  |                               | T <sub>7</sub> (Screening) | T <sub>1</sub> @start | T <sub>8</sub> | T <sub>15</sub> | T <sub>29</sub>  | T <sub>36</sub>          | T <sub>57</sub> (*) @start | T <sub>64</sub> | T <sub>71</sub> | T <sub>85</sub>   | T <sub>92</sub> |
| SELECTION CRITERIA                                   | X                             | X                          | X                     | X              | X               | X  | X                        | X                          | X               | X               | X   | X               |
| INFORMED CONSENT FORM DESIGN                         | X                             |                            |                       |                |                 |  |                          |                            |                 |                 |   |                 |
| PERSONAL DATA  | X                             |                            |                       |                |                 |  |                          |                            |                 |                 |   |                 |
| CLINICAL DATA  | X                             |                            |                       |                |                 |  |                          |                            |                 |                 |   |                 |
| OBJECTIVE EXAMINATION                                | X                             |                            |                       |                | X               |  | X                        |                            |                 |                 | X   | X               |
| DIET   | X                             | X                          | X                     | X              | X               | X  | X                        | X                          | X               | X               | X   | X               |
| BLOOD PRESSURE AND HEART RATE (CLINOSTATIC POSITION) | X                             | X                          | X                     | X              | X               | X  | X                        | X                          | X               | X               | X   | X               |
| DISEASES AND THERAPIES                               | X                             | X                          | X                     | X              | X               | X  | X                        | X                          | X               | X               | X   | X               |
| EFFICACY JUDGEMENT                                   |                               |                            | X                     | X              | X               | X  | X                        | X                          | X               | X               | X   | X               |
| THIGH CIRCUMFERENCE                                  | X                             | X                          | X                     | X              | X               | X  | X                        | X                          | X               | X               | X   | X               |
| SIDE EFFECTS   |                               |                            | X                     | X              | X               | X  | X                        | X                          | X               | X               | X   | X               |
| TOLERABILITY JUDGEMENT                               |                               |                            | X                     | X              | X               | X  | X                        | X                          | X               | X               | X   | X               |

tab. A

[\*]T<sub>57</sub>: ending of the four weeks wash out period and starting of the second treatment period (a) weight only

### RESULTS

All thirty volunteers recruited for the study have completed the treatment.

As shown in tab. A, the two groups [placebo versus test product] resulted to be homogenous towards treatment application, experimental places, population data, vital parameters [SAP, DAP, heart rate].

The average age was 35,6 [age range: 18-60 years old] with prevalence of volunteers ≤40 years old [63% of the population]; percentage of population with age between 40 and 50 years old was 27%, percentage of population between 50 and 60 years old was 10%.



## >> GENERALITIES OF THE CASE STUDY

|                                  | TOTAL (30 cases) |      |      |
|----------------------------------|------------------|------|------|
|                                  | MEDIA ±DS        | MIN  | MAX  |
| AGE (years)                      | 35,6±11          | 18   | 60   |
| TALL (cm)                        | 1,60±0,06        | 1,47 | 1,81 |
| WEIGHT (kg)                      | 62,1±7,5         | 43,2 | 88,1 |
| BMI - BODY MASS INDEX            | 23,1±3,5         | 18,1 | 29,9 |
| AVERAGE THIGH CIRCUMFERENCE (cm) | 55,8±6,6         | 39,4 | 79,5 |

## >> PARAMETERS OF EFFICACY

End point (volunteer efficacy judgment): a progressive **increase of good judgment** was recorded in both groups during the treatment periods; this judgment decreased during the period in which no treatments were performed (wash out and follow up). The highest peak in good judgment was recorded at the end of the second treatment period. As represented in figure one the incidence of positive judgment is higher in the group treated with **Liporedux Pro For Cream** than in the other treated with placebo. **Differences become statistically significant at the end of the second treatment period** and they persist until the end of the follow up period, four weeks after the end of the treatment.



fig. 1

Another confirmation of the trustworthiness of the results comes from the unanimous frequency of the positive efficacy judgments observed in the volunteers.

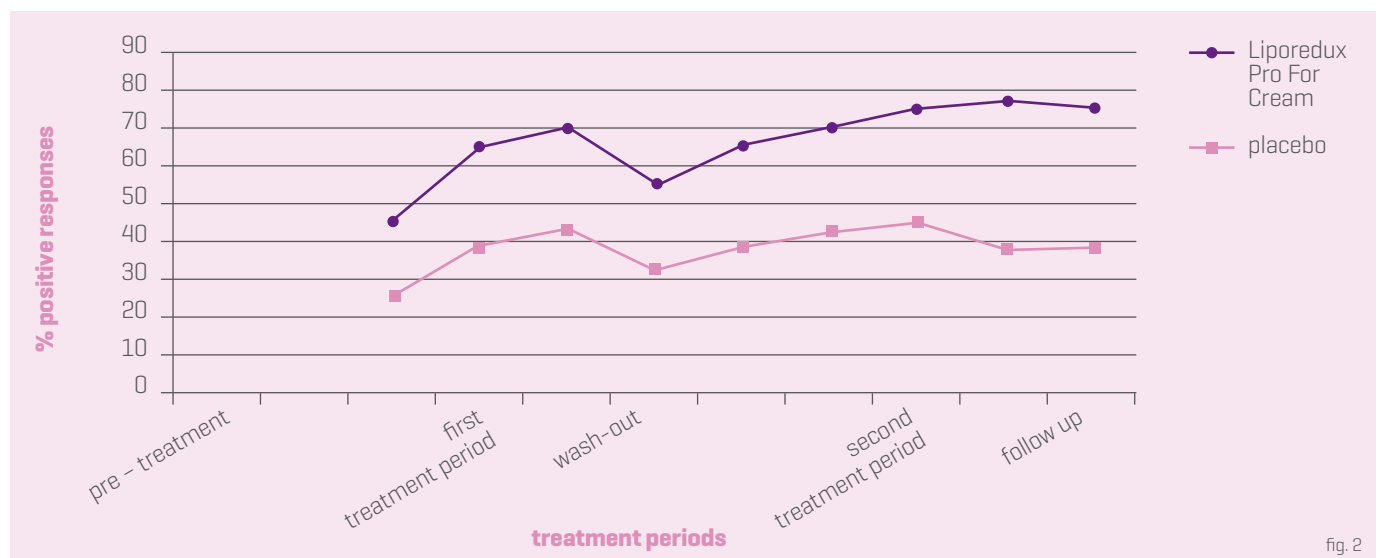


fig. 2

**Thigh Circumference:** results refer to the average circumference of both volunteer's thighs.

During the run in week, in which volunteers didn't undergo topic or systemic treatments to decrease fatty deposits or change their diet and life style, average circumference was stable. During treatment periods both products were able to decrease the average circumference, with a higher efficacy during the second period of treatment.

In the wash out and follow up weeks, after the first and second treatment periods respectively, a loss of results achieved was observed (fig. 3).

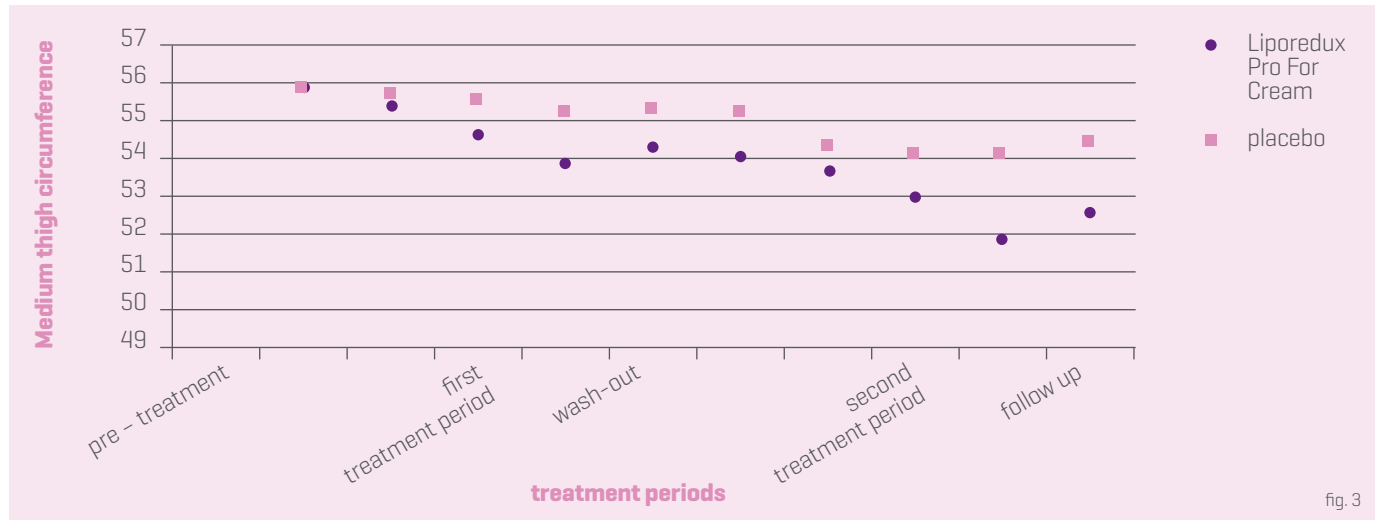


fig. 3

Decrease in the average thigh circumference appears directly related to the duration of the treatment and to the number of the treatment periods (cycle): reduction effects achieved in the second period were more significant than the effects obtained after the first treatment period (fig. 4).

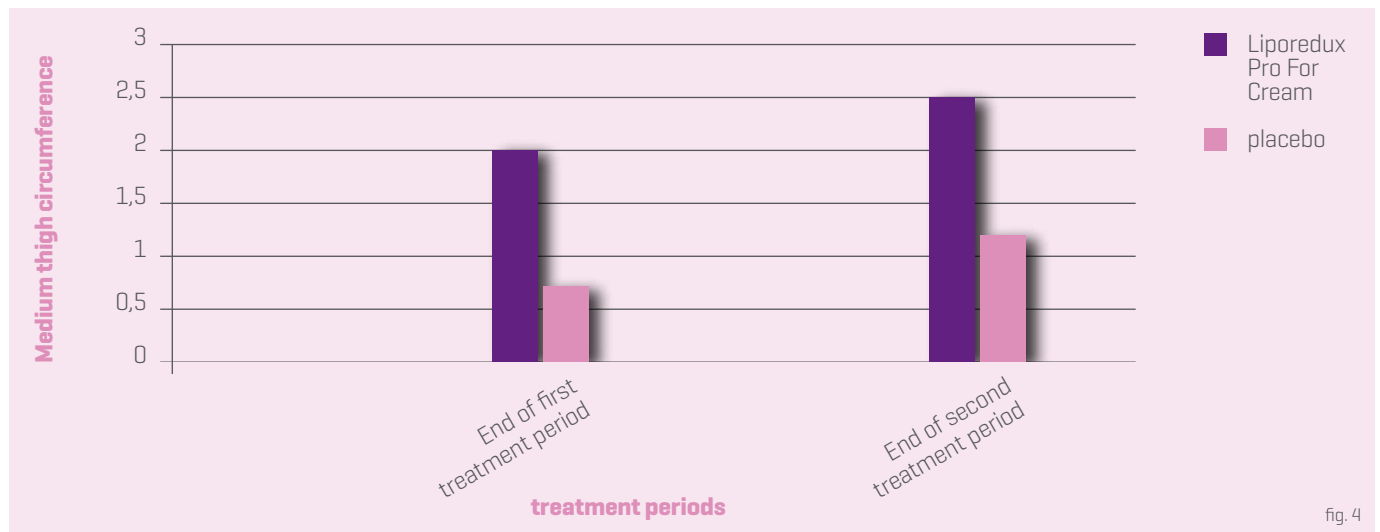


fig. 4

Comparison between the two groups shows that decrease of thigh circumference in volunteers treated with **Liporedux Pro For Cream** is higher than in volunteers treated with placebo, with an endpoint at the end of second treatment period of

**2,34 cm [-4,17%]**

versus only 1,52 cm in volunteers treated with placebo. The more significant differences emerge from statistical analysis.

**Weight (Kg):** during study volunteers didn't modify their lifestyle or diet exhibiting no significant modifications in basal weight. Reductions of average thigh circumference value cannot therefore be considered to a loss of weight.

## Tolerance profile

**Vital Parameters:** during the two treatment periods using the two products no significant modifications in blood pressure and heart rate were observed in comparison to the periods in which no treatment was performed.

**Side effects:** no local side effects or allergic manifestations in the zones of application of the product were recorded among volunteers during treatment period.

**Tolerability judgments:** **95% of volunteers defined "good"** the tolerability of the treatment versus a 5% who defined the tolerability "sufficient". Judgment of the Doctor was in accord with the volunteer.

## >> CONCLUSIONS

Results obtained show that the treatment with **Liporedux Pro For** produces a **more significant effect on cellulite** in comparison to the placebo treated control group. **Cellulite reduction increases gradually during the treatment periods;** the effects were more remarkable in the second treatment period than in the first one and they persist for the successive weeks of follow up.

These results were obtained evaluating the main parameter, the judgment expressed by the volunteers about treatment efficacy; this main result was supported by reduction of the circumference of both thighs, considered as secondary efficacy (or activity) parameter.

Differences between the two groups of volunteers, the one treated with the test product and the other treated with placebo depends from the duration of treatment and from the number of treatment cycles, reaching the statistic significance at the end of the second period for the main and the secondary parameter.

The tolerability of the product is good since no heart rate or blood pressure modifications were recorded during the study. No side effects on the skin were observed.

**It can be assessed therefore that this controlled, randomized, double-blind study performed on a wide sample of volunteers affected by edematous fibrosclerotic panniculopathy of the thighs underlined and confirmed the higher efficacy of the product in comparison to the placebo and furthermore its good local and systemic tolerability also if used for prolonged treatments and repeated cycles.**

## >> PRODUCT SPECIFICATIONS

| INCI NAME and COMPOSITION:     | CAS No | EINECS / ELINCS | RANGE % |
|--------------------------------|--------|-----------------|---------|
| CARNITINE ISOMERIZED LINOLEATE | -      | -               | <25 ≥10 |
| COLEUS FORSKOHLII ROOT EXTRACT | -      | -               | <5 ≥1   |

| PHYSICAL - CHEMICAL CHARACTERISTICS | LIMITS                  |
|-------------------------------------|-------------------------|
| APPEARANCE                          | VISCOUS FLUID LIQUID    |
| COLOUR                              | COLOURLESS/STRAW YELLOW |
| ODOUR                               | SLIGHT TYPICAL          |
| pH DIRECT                           | 7 - 9                   |
| PROTEIC NITROGEN                    | 0.45 - 0.55             |
| IDENTIFICATION FORSKOLIN (HPLC)     | COMPLIES                |
| TOTAL MICROBE COUNT                 | 0 - 100                 |

**LIPO**  **REDUX**  
PRO FOR



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