ACTIPORINE 8.G

Cellulite Innovation

Actiporine 8G

Cellulite Innovation

MARKET REALITY: SMOOTHING OUT CELLULITE TO RECONCILE WITH YOURSELF

90% of women have cellulite, and nearly 33% of them make it a daily obsession. For most of them, the goal is to smooth out cellulite to reconcile with themselves. In this market, full of expectations, consumers are increasingly looking for innovative cellulite strategies.

A UNIQUE ACTION MECHANISM

By maintaining mitochondrial homeostasis in adipocytes and fibroblasts, Actiporine 8G promotes not only the elimination of fats but also the synthesis of collagen, to smooth out dimples. Its mechanism of action is unique. It targets mitochondrial Aquaporin 8 which is responsible for transporting H202 from the inside of mitochondria to the outside. By freeing mitochondria of this toxic substance, Actiporine 8G maintains their physical and functional integrity and restarts the original cellular activity of adipocytes, i.e. lipolysis as well as collagen synthesis by the fibroblasts. Dimples are therefore reduced and smoothed out.

A TECHNOLOGIC INNOVATION INITIATED IN 2006: THE CULTIVATION OF JANIA RUBENS

Jania comes from the Latin Janus, the two-headed god of Roman mythology, guardian of the House of the Gods. Rubens means the colour red. The alga was given this name due to its dichotomous branching and its colour. Jania Rubens is a calcified alga that grows from 15 to 40 mm in height. It is fairly rare and grows in well-lit areas, on underwater rocky surfaces and also on marine sandy floors and in marine zostera herbaria.

To prevent removal of this rare resource from its natural habitat, our laboratory has been the first one to develop cultures in a photobioreactor with controlled temperature, light and culture media. The algae obtained using this method have the shape of a pompon, similar to that observed in their natural habitat, but without any epiphytes. The extract obtained from it: Actiporine 8G is guaranteed to be 100% natural and to have no traces of impurities.

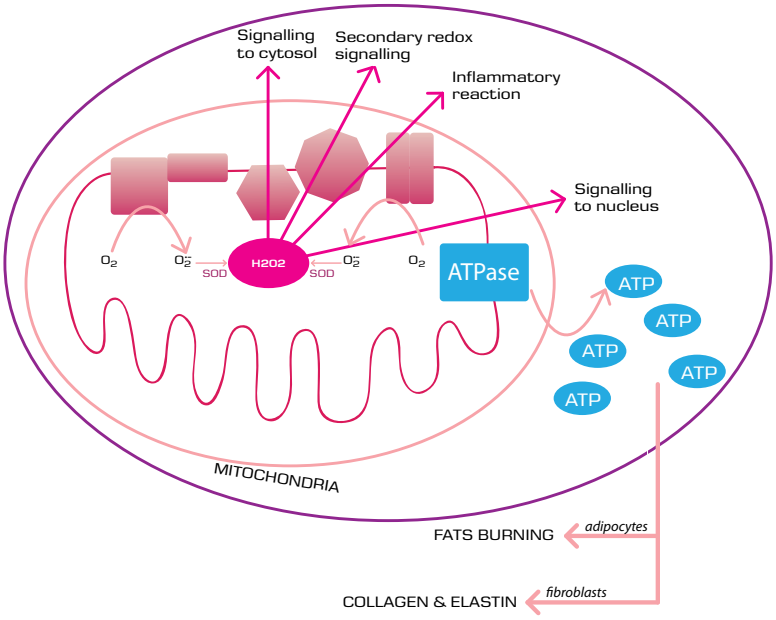
MITOCHONDRIAL HOMEOSTASIS- AQUAPORIN 8 – LIPOLYSIS – COLLAGEN – CAPITONS

CELLULITE : IMPORTANCE OF MITOCHONDRIAL HOMEOSTASIS

ROLE OF MITOCHONDRIA IN ANTI-CELLULITE STRATEGIES.

Cellulite is mainly due to 2 phenomena: increase in fats storage into adipocytes and distortion of the collagen fibres which surround the adipocytes. Smoothing out cellulite consists in deflating the adipocytes by activating lipolysis and firming the underlying tissues by stimulating collagen synthesis.

These two processes are connected to the integrity, vitality and thus energy reserves of the adipocytes and fibroblasts. However the only source of energy available to the cells is ATP, which is synthesised by the mitochondria.



IMPORTANCE OF MITOCHONDRIAL HOMEOSTASIS IN ANTI-CELLULITE STRATEGIES

It is now well known that mitochondrial DNA, due to its closeness to reactive oxygen species, and mainly H202, is continually subject to damages and mutations leading to mitochondrial malfunction and loss of cellular vitality. However H202 is a messenger of vital importance in a large number of metabolic reactions.
Therefore it is important to remove H202 from the mitochondria without, however, completely eliminating it.

It is necessary to ensure a balance (or mitochondrial homeostasis), in the fibroblasts and adipocytes so that they function correctly.

THE ROLE OF AQUAPORINE 8 IN MITOCHONDRIAL HOMEOSTASIS

Aquaporins belong to a large family of cellular channels with members in all kingdoms of life, and known as efficient water channels. They can be found in the cellular membrane, mitochondrial membrane or cytosol.

Aquaporine 8 (AQP8) has been discovered in keratinocytes in 2008 by Codif International. It is now well known in cosmetics for its hydration function. Recently, Biernet and al [1] discovered a new function of AQP8 in transporting H2O2 from matrix mitochondria to the cytosol.

Carrying on this work, Codif International then localised AQP8 in adipocyte and fibroblast mitochondria and made the connection between AQP8 and mitochondrial homeostasis.

DEMONSTRATION

Evidence of AQP8 synthesis in mitochondria of human adipocytes and human fibroblasts by Codif International laboratories.

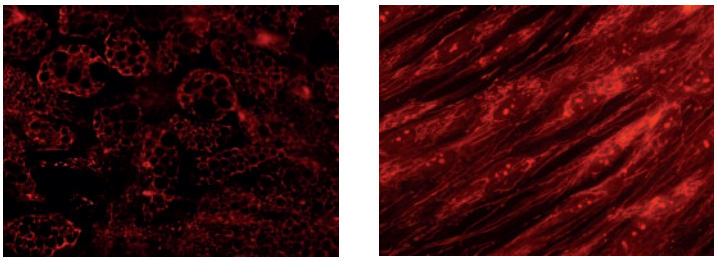
Protocol :
Left side: culture of differentiated human adipocytes. Right side : culture of human fibroblasts
Labelling of mitochondria in red
Labelling of AQP8 in green
Co-labelling of mitochondria and AQP8 in orange

RESULTS

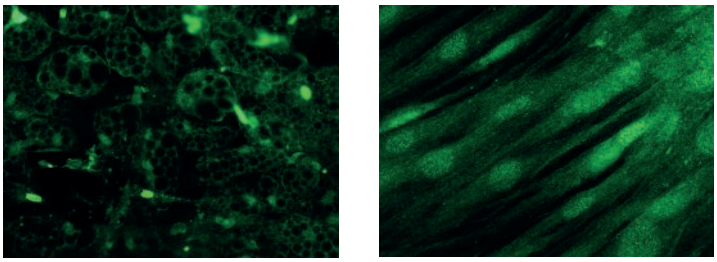
The colabelling of mitochondria and AQP8 put in evidence the synthesis of AQP8 into mitochondria of human adipocytes and human fibroblasts.

The stimulation of AQP8 synthesis should be translated by a strengthening of mitochondrial homeostasis, and therefore a reactivation of lipolysis by adipocytes as well as a reactivation of collagen synthesis by fibroblasts.

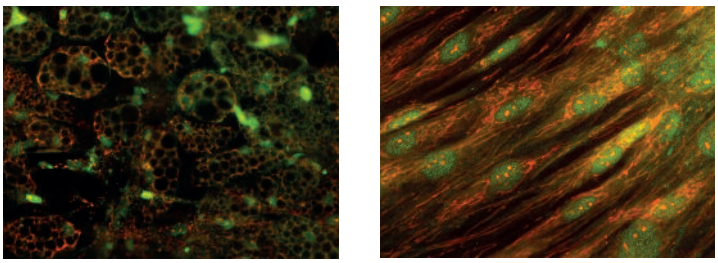
Adipocytes culture **Fibroblasts culture**



Labelling of mitochondria in red



Labelling of AQP8 in green



Co-labelling of mitochondria and AQP8 in orange

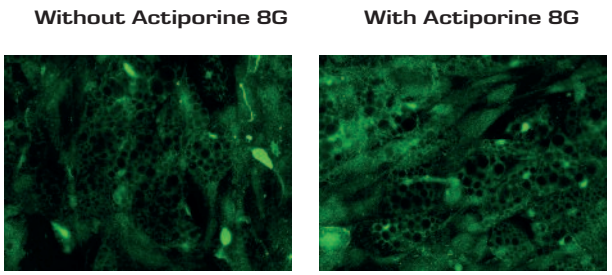
(1).Biernert, G. P., and Moller, A. L. (2006) J. Biol. Chem 282, 1183-1191

IN-VITRO TESTS: EFFECT OF ACTIPORINE 8G ON ADIPOCYTES

ANTI-CELLULITE HEALING EFFECT

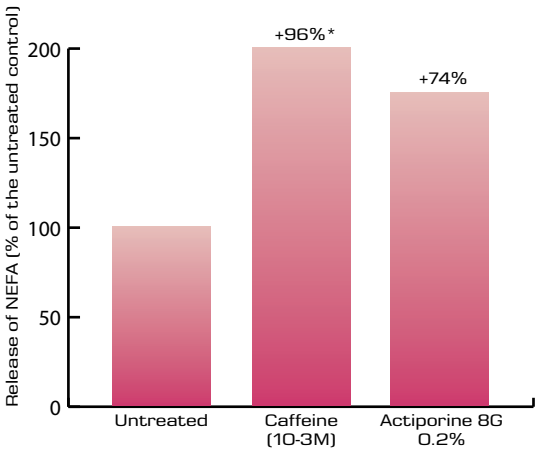
ACTIPORINE 8G STIMULATES THE SYNTHESIS OF AQP8 INTO ADIPOCYTES BY +50%*.

Induction of differentiation of pre-adipocytes with or without 0.2% Actiporine 8 G. Marking and quantification of AQP8 after 3 weeks.
+50%* AQP8 synthesis in cultures treated with Actiporine 8G.
(*p<0.05 Student test).



ACTIPORINE 8G STIMULATES LIPOLYSIS BY +74% INTO DIFFERENTIATED ADIPOCYTES.

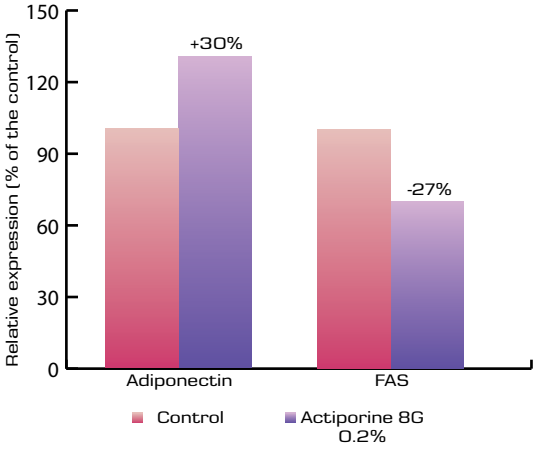
Human mesenchymal stem cells differenciated into adult adipocytes and treated with 0.2% Actiporine 8G or 10-3 M caffeine. Quantification of non esterified fatty acids (NEFA) released into the culture medium after 2 hours.
+74% fatty acid release by adipocytes treated with Actiporine 8G.
(*p<0.05 test de Student).



ANTI-CELLULITE PREVENTIVE EFFECT

ACTIPORINE 8G CONTROLS FATS STORAGE AND THE EXPANSION OF THE ADIPOSE TISSUE.

In addition to its lipolytic and firming effect, Actiporine 8G stimulates adiponectin synthesis by 30% (adipokin which controls the growth of adipose tissue), and inhibits fatty acid synthase (FAS) expression, the enzyme involved in fatty acid synthesis, by 27%.

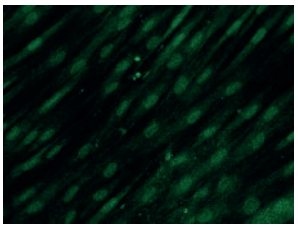


IN-VITRO TESTS: EFFECT OF ACTIPORINE 8G ON FIBROBLASTS

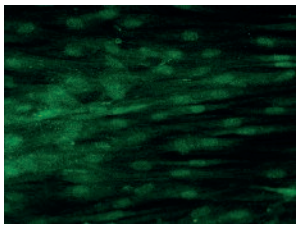
ACTIPORINE 8G STIMULATES AQP8 SYNTHESIS INTO FIBROBLASTS BY +58%*

Human dermal fibroblasts (female 37 years old) cultivated with or without 0.2% Actiporine 8G. Marking and quantification of AQP8 after 24 hours.
+58%* AQP8 in cultures treated with Actiporine 8G.
(*p<0.05 Student test)

Without Actiporine 8G

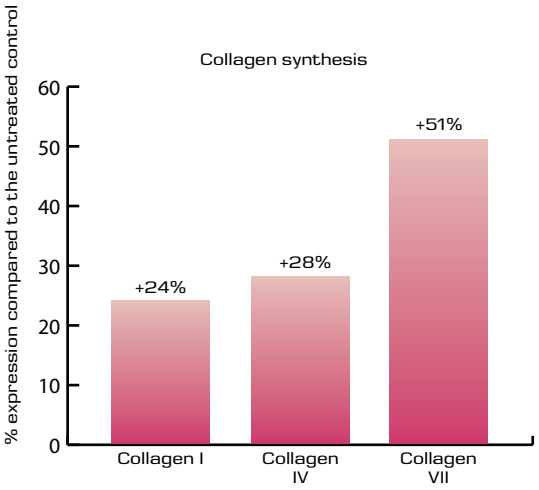


With Actiporine 8G



ACTIPORINE 8G STIMULATES THE SYNTHESIS OF COLLAGEN I : +24%, COLLAGEN IV : +28% AND COLLAGEN VII : +51%

Human dermal fibroblasts (female 37 years old) cultivated with or without 0.2% Actiporine 8G. Collagen I quantified by immuno-marking and Collagen IV and VII with mini-chips.
+24% collagen I, +28% collagen IV, +51% collagen VII.



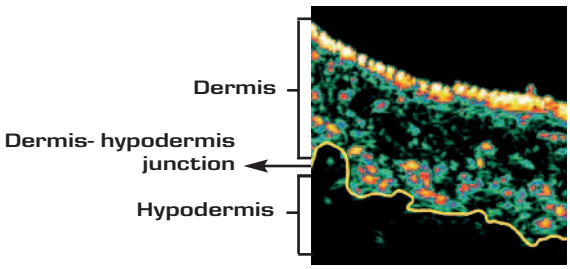
By stimulating the synthesis of AQP8 into adipocytes, Actiporine 8G maintains mitochondrial homeostasis and reactivates lipolysis by adipocytes. This action allows the decrease of adipocytes volume. Meanwhile, the stimulation of adiponectine synthesis as well as the inhibition of fatty acids synthase lead to the control of adipose tissue expansion and avoid the reappearance of capitons.

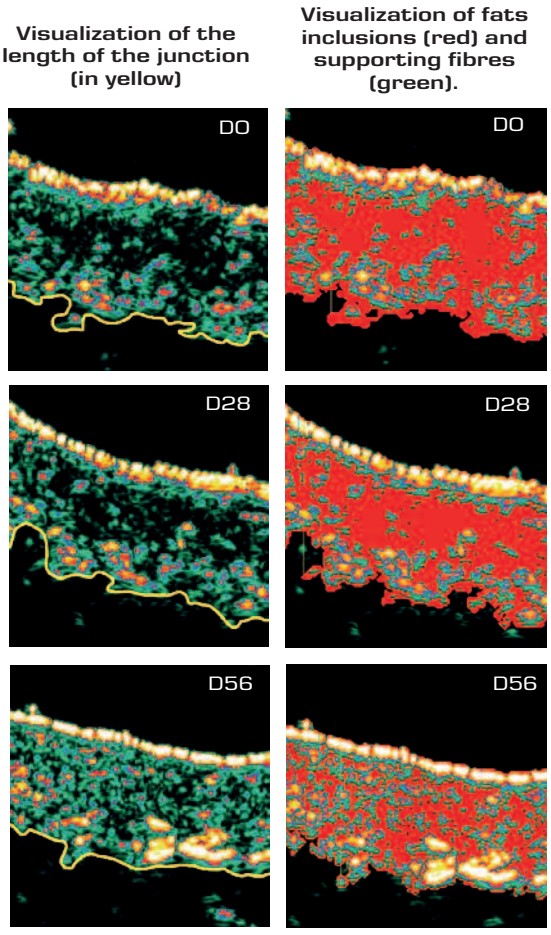
By stimulating AQP8 synthesis by fibroblasts, Actiporine 8G maintains mitochondrial homeostasis and reactivates the synthesis of collagen I, IV and VII. This action firms dermis and smoothes out cellulite.

Protocol:
20 volunteers with cellulite on the thighs.
Application of a cream containing 2% Actiporine 8G on one thigh and a placebo on the other one.
Treatment duration: 8 weeks.

ECHOGRAPHIC ANALYSIS OF THE LENGTH OF THE DERMIS-HYPODERMIS JUNCTION AND FATS INCLUSIONS INTO THE DERMIS.

When they grow, adipocytes distort and enlarge the dermis-hypodermis junction and invade the dermis by forming fatty inclusions. Therefore an effective lipolytic and firming action must be achieved by reducing the length of the junction as well as by reducing the number of fatty inclusions in the dermis, promoting instead an increase in the support fibres.





RESULTS AFTER 28 DAYS OF TREATMENT

Length of the junction:
-11% on average versus placebo and up to -46%

Fats inclusions:
-3% on average versus placebo and up to -24%

RESULTS AFTER 56 DAYS OF TREATMENT

Length of the junction:
-18%* on average versus placebo and up to -64%
*p<0.05 Student test

Fats inclusions:
-7%* on average versus placebo and up to -25%
*p<0.05 Student test

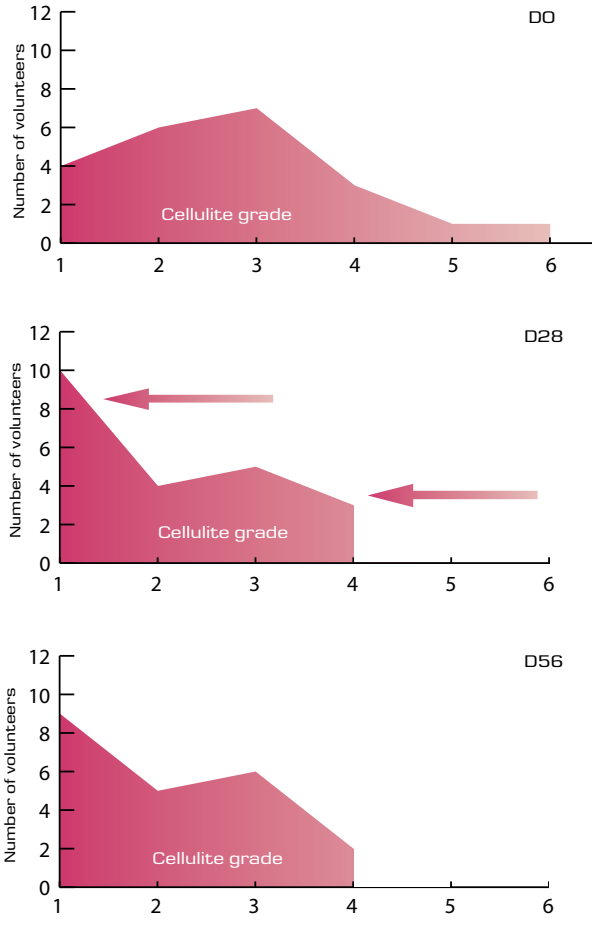
ANALYSIS OF CELLULITE GRADE

The impact on orange peel effect has been evaluated thanks to a visual scoring of cellulite on not pinched thighs, using 10 points scale.

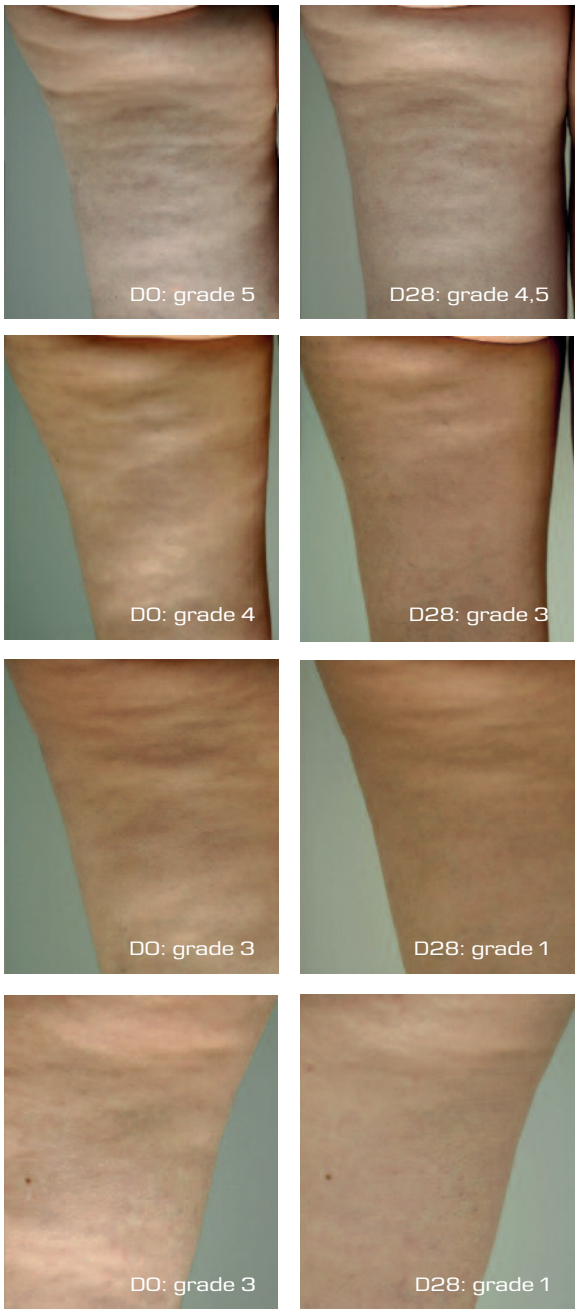
VARIATION OF CELLULITE GRADE DURING THE TREATMENT

After 28 days:
-10% on average versus placebo and up to -67%
After 56 days:
-15%* on average versus placebo and up to -75%
*p=0.05 Student test

VOLUNTEERS DISTRIBUTION WITH REGARDS TO THEIR CELLULITE GRADE DURING THE TREATMENT



VISIBLE RESULTS



Due to its unique action mechanism on AQP8, Actiporine 8G restores mitochondrial homeostasis in adipocytes and fibroblasts and reactivates lipolysis and collagen synthesis. Fatty inclusions are eliminated, the dermis regains its firmness and dimples are visibly smoothed out.

Marine origin | Hydrosoluble active ingredient | In-vitro test | In-vivo test | Cosmos validation | Controlled management program of natural resources

FORMULATION GUIDELINE / SLIMMING BI-GEL

This bi-gel is formulated with Actiporine 8G and a draining active ingredient : Rhodofiltrat Palmaria G.

Phase	Raw material / commercial name	INCI name	%
A	ELMULFREE CBG (1)	Isotearyl Alcohol & Butylene Glycol Cocoate & Ethylcellulose	4
	LANOL 99 (2)	Isononyl Isononanoate	5
	LEXFEEL D5 (3)	Neopentyl Glycol Diheptanoate & Isododecane	4
	PHENOXYETHZNOL (4)	Phenoxyethanol	0,75
	DERMOSOFT OCTIOL (5)	Caprylyl Glycol	0,25
A'	LANOL 99 (2)	Isononyl Isononoate	1
	UNIPURE RED LC 381HLC (6)	CI 77491 & Hydrogenated Lecithin	0,0014
	UNIPURE YELLOW LC 182 HLC (6)	CI 77492 & Hydrogenated Lecithin	0,00165
B	EAU DÉMINÉRALISÉE	Aqua	73,427
	CARBOPOL ETD 2020 (7)	Acrylates/C10-30 Alkyl Acrylate Crosspolymer	0,4
	ELESTAB CPN (8)	Chlorphenesin	0,27
C	GLYCÉRINE BIDISTILLÉE CODEX (9)	Glycerin	3
	XANTHAN GUM (10)	Xanthan Gum	0,2
D	SOUDE (11)	Aqua & Sodium Hydroxide	0,6
E	**ACTIPORINE 8G (12)**	**Glycerin & Aqua & Jania Rubens Extract**	**2**
	RHODOFILTRAT PALMARIA G (12)	**Glycerin & Aqua & Palmaria Palmata Extract**	**5**
	PARFUM FLEUR ET FRUIT 0217350	Parfum	0,1

(1) Gattefossé, (2) Seppic, (3) Inolex, (4) Laserson, (5) Dr Straetmans, (6) Sensient LCW, (7) Lubrizol, (8) Cognis, (9) Quimasso, (10) Jungbunzlauer, (11) Brenntag, (12) CODIF Recherche et Nature, (13) Expressions parfumées Formulation CLVALG800MP

PRODUCT ASPECT: Pink glitter bi-gel

PRODUCT PROPERTIES: pH = 6.45 ± 0.3

PROTOCOL:

- Prepare A in deflocculating. Check that the mixture is homogeneous and clear.
- Heat the water to 70 ° C to disperse the Carbopol emulsifier under 1500 rpm for 15 min.
- Introduce Elestab CPN. Mix 5 minutes. Cool to 35 ° C.
- Then add the emulsifier premix C under 2000 rpm for 10 min.
- Neutralize with D as emulsifier 2000 rpm for 10 min.
- Insert A into B emulsifier slowly under 2500 rpm, then let stir under these conditions for 15 min.
- Add E.

ACTIPORINE 8G : CELLULITE INNOVATION

Cosmetic activities

- Stimulates mitochondrial AQP8 synthesis into adipocytes and fibroblasts
- Stimulates lipolysis and fatty acids release
- Stimulates the synthesis of collagen I, IV and VII
- Stimulates the synthesis of adiponectin
- Inhibits the synthesis of fatty acids synthase
- Decreases the length of dermis-hypodermis junction
- Decreases the number of fats inclusions into dermis
- Decreases cellulite grade and smoothes out capitons

INCI name

Glycerin (and) Water (and) Jania Rubens extract - ! CHINESE COMPLIANT!

% of use recommended: 2%