

# GLUTRAPEPTIDE<sup>®</sup>



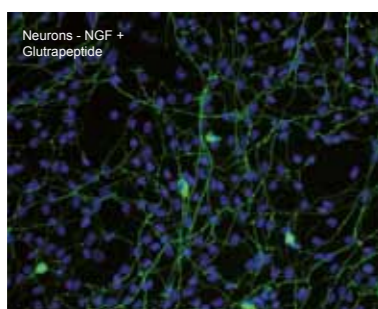
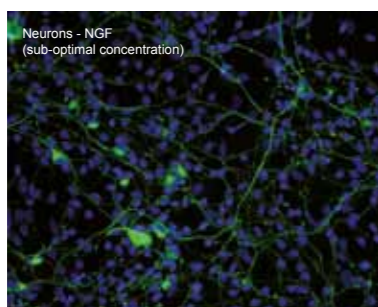
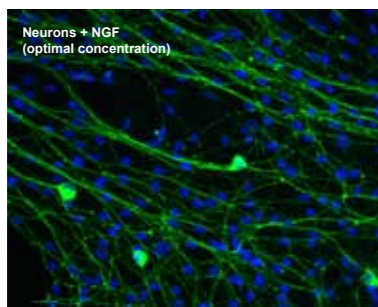
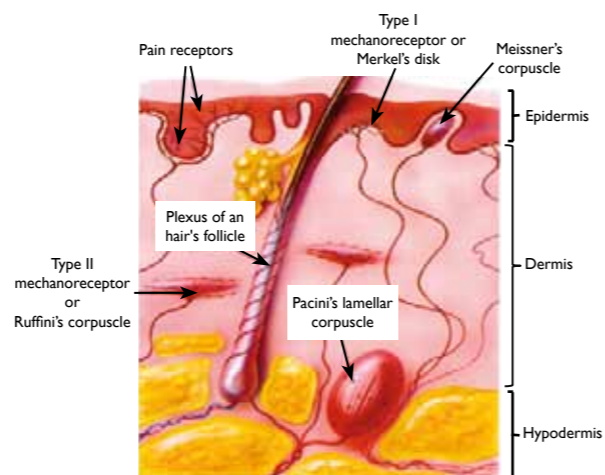
NEUROSlimMING  
NEUROPROTECTION  
ANTI-OXIDATION

**EXSYMOL**  
MONACO

## NEUROPROTECTION

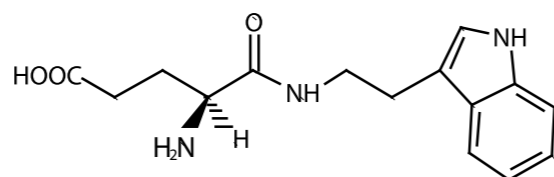
The skin is a highly innervated tissue. Indeed, it has been shown that neurons have connections with each of its compartments: the epidermis, the dermis and the hypodermis. Hence, the nervous cells form a network and therefore communicate with keratinocytes, fibroblasts and adipocytes respectively.

Nerve Growth Factor (NGF) is a protein synthesized by keratinocytes, fibroblasts and adipocytes in the skin. Its role is to promote neuron differentiation and survival. However, with age, the levels of NGF decrease, hence the neurons tend to dedifferentiate and to ultimately die. Neurons are fragile cells which can hardly proliferate. It is therefore extremely important to protect them.



The neurons are protected, the skin is younger

As pioneers in cosmetic applications, Exsymol developed **GLISTIN**, a neuroprotector with anti-oxidative properties. It was shown that **GLISTIN**, by protecting neuronal cells, is able to enhance keratinocytes' resistance to UV radiations and to upregulate the expression of genes involved in the barrier function.



**GLISTIN, FORMER GENERATION OF NEUROPROTECTOR**

**GLUTRAPEPTIDE** is a second generation neuroprotector. It potentializes neuronal response to NGF and therefore slows down the neurodegenerescence induced by the decrease of NGF levels.

Unlike **GLISTIN**, which main purpose is to protect the nervous network within the superficial layers of the skin for a stronger efficacy on the epidermis, **GLUTRAPEPTIDE** was designed to reach the deepest layers of the skin where adipocytes are located. Hence, **GLUTRAPEPTIDE** is able to protect deep nerve endings, therefore allowing an optimal lipolysis by adipocytes.

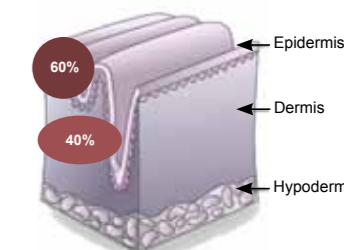


INCI name: PYROGLUTAMYLAMIDOETHYL INDOLE

Designed and engineered for maximum bioavailability throughout the whole skin tissue, **GLUTRAPEPTIDE** displays a 10 fold superior penetration capacity when compared with caffeine, and a 5,000 fold increase when compared with **GLISTIN**. As a result, more than 40% of the penetrating **GLUTRAPEPTIDE** is able to reach the dermis after cutaneous application.

### Skin benefits

- **Neuroprotection**  
Protects neurons from the NGF drop-induced neurodegenerescence. (Exsymol, 2007 – DO\_1086).
- **Neuroslimming - Neurolipolyse**  
Enhances the neurons ability to support the lipolysis process by the adipocytes. (Exsymol, 2010)  
Glutrapeptide for fighting chronic emotional stress-induced fat accumulation. (Exsymol, 2014).
- **Body firming**  
Enhances fibroblast contractile ability (Exsymol, 2010 – PRS0108, Internal data).
- **Cell detoxification**  
Global anti-oxidative properties (Exsymol, 2007 – DO\_1085).  
High affinity for hydroxyl radical (Exsymol, 2007 – DO1076).



Penetration index (Log P)	
<b>GLUTRAPEPTIDE</b>	<b>+1.03</b>
<b>GLISTIN</b>	<b>-2.7</b>
Cafeine	-0.07

### Cosmetic applications

- Slimming and firming agent
- Anti-cutaneous neurodegenerescence
- Anti-aging
- Anti-oxidation

# GLUTRAPEPTIDE

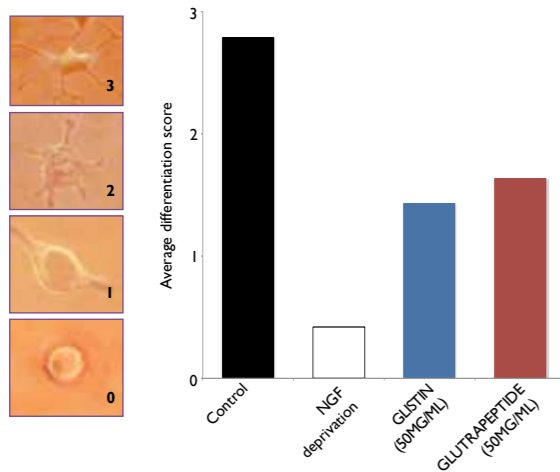
## Experimental research : *in vitro*

### GLUTRAPEPTIDE is a potent neuroprotector

With age, NGF levels decrease and neurons undergo a dedifferentiation process: they shrink and ultimately die.

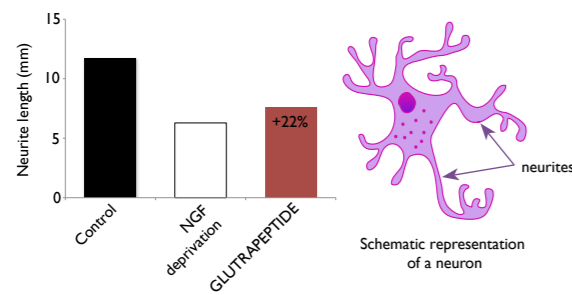


Using a scoring method depending on the differentiation stage of the neuronal cells (from a score of 3 for a fully differentiated cell to a score of 0 for an undifferentiated one), we measured the protecting effect of GLUTRAPEPTIDE against this neurodegeneration.



GLUTRAPEPTIDE protects the neuronal cells from the dedifferentiation process occurring in response to a drop of NGF levels.

We confirmed these results by measuring the average length of the cells' neurites. Hence, treatment with GLUTRAPEPTIDE provided a 22% protection against neurite shrinkage.

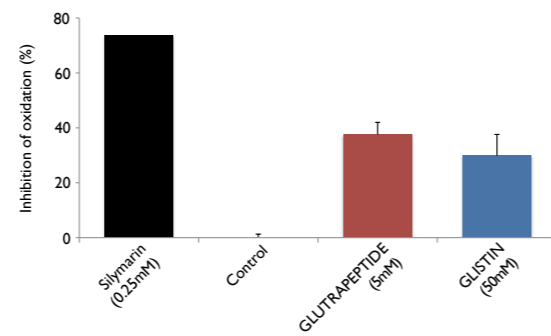


The nervous system is protected.  
The cross-talk between the skin cells is preserved.

### GLUTRAPEPTIDE is a potent anti-oxidant

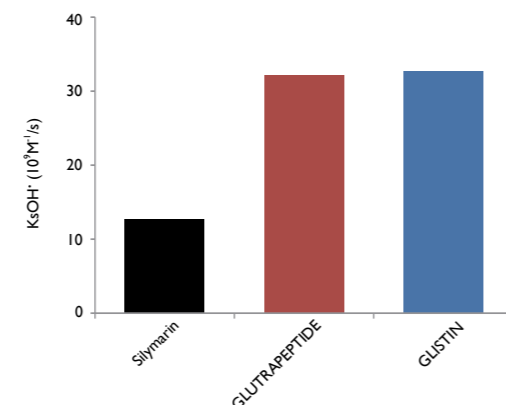
We assessed GLUTRAPEPTIDE's ability to protect the cells from oxidative stress by measuring its global anti-oxidative properties for different types of radicals (ROS, RCS and RNS).

GLUTRAPEPTIDE has anti-oxidative properties as high as GLISTIN. Furthermore, there is a trend suggesting that GLUTRAPEPTIDE is even more potent than its parent compound: Glistin.



We also assessed GLUTRAPEPTIDE's ability to specifically neutralize the hydroxyl radical (OH•) that has been shown to be the most reactive free radical.

Similarly to GLISTIN, GLUTRAPEPTIDE is extremely efficient at scavenging OH• radicals. As a result, it provides a reliable protection against oxidative stress.



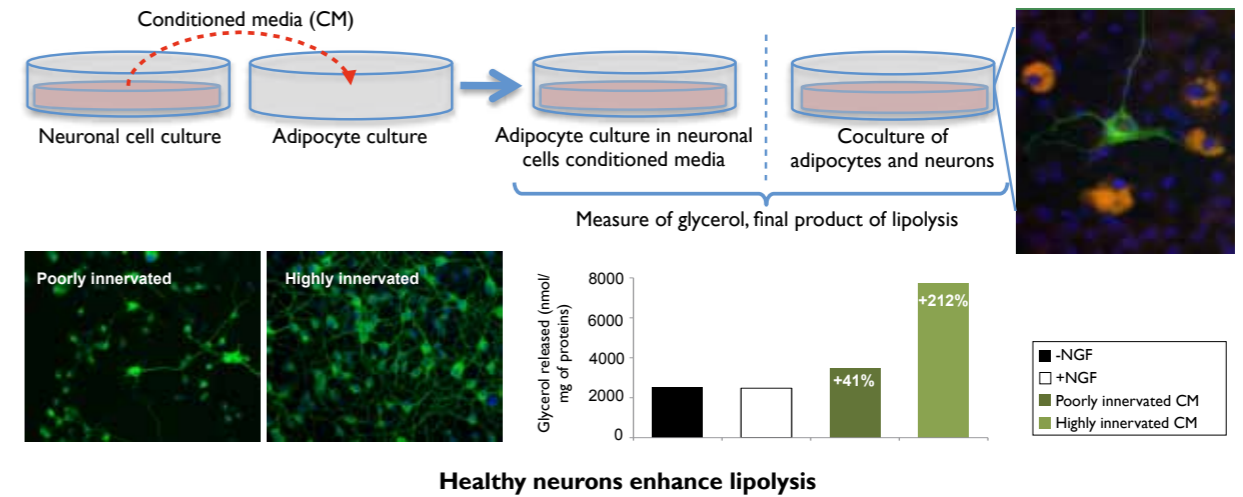
The skin is protected, healthier.

# GLUTRAPEPTIDE

## Neuroslimming

### NEUROSLIMMING : Principle

Previous investigations showed that the adipose tissue is highly innervated and that the nerve endings form a complex network between adipocytes and neurons. It was also shown that the more innervated the tissue is, the more efficient the lipolysis is. Taken together, these data show that healthy neurons secrete neuromediators (norepinephrin) capable of enhancing adipocytes' ability to perform the lipolysis process as assessed by coculture (a model of adipose tissue) and conditioned media assays.



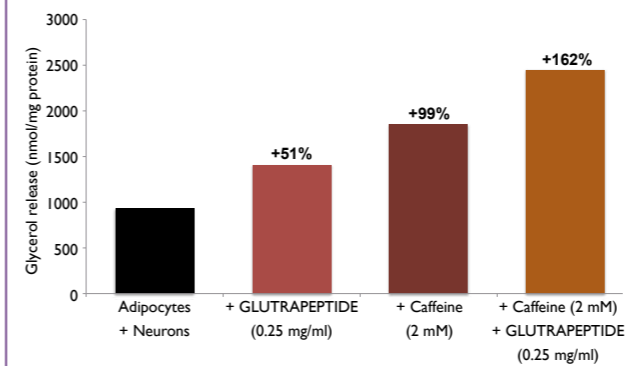
Healthy neurons enhance lipolysis

### GLUTRAPEPTIDE enhances neurons' ability to support lipolysis

Healthy neurons secrete neuromediators responsible for an enhanced lipolysis from adipocytes.

We showed that GLUTRAPEPTIDE is able to prevent the neurodegeneration in a NGF-like way. Hence, a treatment with GLUTRAPEPTIDE extends the viability and the metabolic abilities of neuronal cells.

Neurons have their ability to support lipolysis enhanced when in the presence of GLUTRAPEPTIDE. Furthermore, when GLUTRAPEPTIDE is used together with caffeine, the adipose tissue can enjoy the double effect of the caffeine and the neuron-induced lipolysis enhancement.

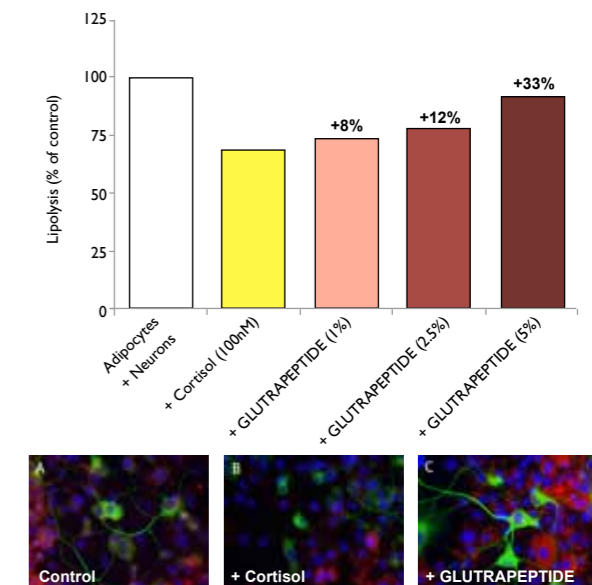


The neuron-induced lipolysis is potentialized and there is a synergy with caffeine for slimming benefits

### GLUTRAPEPTIDE reduces stress-induced fat accumulation

Because of chronic emotional stress (caused by job strains, sleep deprivation...), the body produces cortisol. This corticoid can have a dual noxious effect as it can dramatically boost appetite, and promote fat storage while strongly reducing lipolysis.

In a neurons (green) / adipocytes (red) coculture, we show here that GLUTRAPEPTIDE is capable of reducing stress-induced, cortisol-mediated fat accumulation by improving neuron survival.



GLUTRAPEPTIDE fights the noxious effects of chronic emotional stress

# GLUTRAPEPTIDE

## Neuroslimming: From lab to live

# GLUTRAPEPTIDE

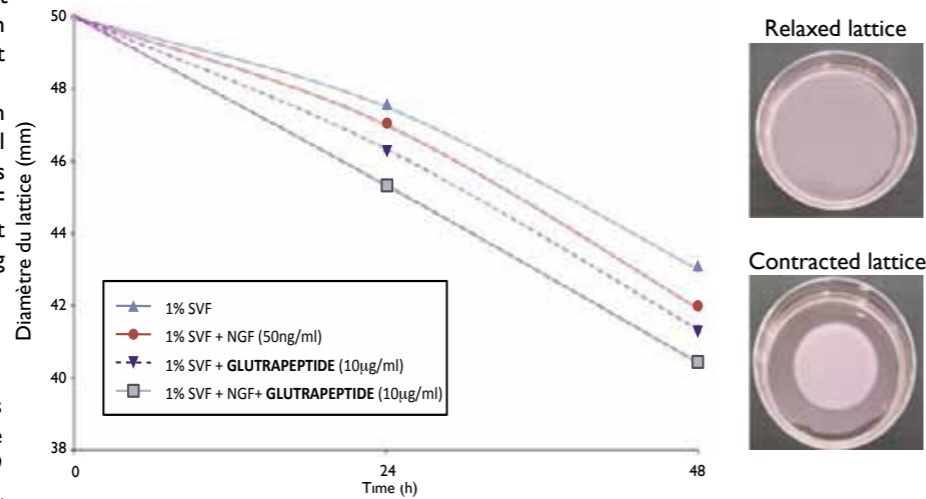
## Technical Characteristics

Realized under dermatological control, this study was performed on 49 volunteering women aged between 30 and 50.

*In vitro* studies have shown that GLUTRAPEPTIDE acts together with NGF in order to enhance fibroblast contractile ability. We showed that the contraction of lattice in a low serum level media, a model of aged dermis, was quicker in the presence of both NGF and GLUTRAPEPTIDE, suggesting that GLUTRAPEPTIDE also has firming properties.

In order to confirm GLUTRAPEPTIDE's firming and slimming properties, we performed an *in vivo* assay on 49 volunteering women aged 30 to 50.

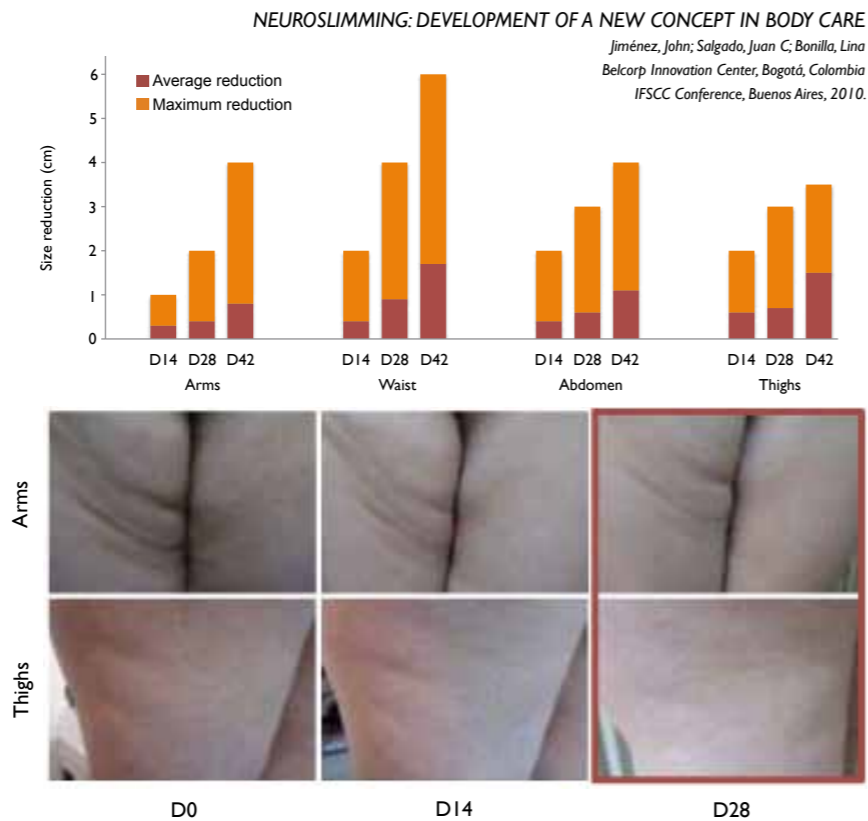
After 14, 28 and 42 days of treatment with GLUTRAPEPTIDE (3%) twice a day, a dermatologist measured the size of several body parts (arms, waist, abdomen and thighs) and assessed the firmness and quality of the skin.



After 28 days of treatment, all volunteers observed an amelioration in cellulite appearance.

A dermatologist measured the size of several body parts before and after the treatment with GLUTRAPEPTIDE and observed an overall slimming effect that could reach up to 4cm for the arms, 6cm for the waist, 4cm for the abdomen and 3.5cm for the thighs.

An improvement of the skin appearance, firmness, density and elasticity was also observed by a dermatologist after the 28 day treatment with GLUTRAPEPTIDE.



**GLUTRAPEPTIDE has slimming and firming effects as measured on volunteers by a dermatologist.**

### ANALYTICAL COMPOSITION

Pyroglutamylamidoethyl indole.....1% (w/w)  
Butylene glycol.....30%  
Water (sq).....100%

### TECHNICAL CHARACTERISTICS

Limpid, colorless liquid  
pH ≈ 6,0  
Density at 20°C ≈ 1.0  
Miscible with water, alcohols and glycols.

### PRESERVATIVES

No preservatives.

### TOLERANCE & TOXICITY STUDIES

GLUTRAPEPTIDE is perfectly tolerated. Tolerance and toxicity studies were performed using both *in vitro* (cell culture and reconstructed epidermis) and *in vivo* (human volunteers) methods.

### FORMULATION

Advised doses : 1 to 5%.  
GLUTRAPEPTIDE is not temperature sensitive. In order to avoid faint discoloration of the solution, it is recommended to store GLUTRAPEPTIDE away from the light.

### AVAILABILITIES

GLUTRAPEPTIDE is available in 1, 5 and 30kg drums.

