[F-BTX]

Product identity

F-BTX is the ultimate treatment to achieve the best results in a shortest time. Each vial is containing the pure active ingredients only, without any preservatives or other chemicals. It combines 2 generations of peptides (Octapeptides & Pentapeptides) with a botox-like effect. The peptides inhibit and reduce facial contractions, preventing the formation of new expression lines and reducing the appearance of wrinkles. A unique synergy for a total lifting effect.

Benefits

- Reduces wrinkles & fine lines.
- Reduces expression wrinkles.
- Stimulates collagen synthesis.
- Firms the skin.
- Moisturizes.
- Replaces botox & hyaluronic acid microinjections.

Active ingredients

- Octapeptides & pentapeptides.
- Hyaluronic acid low-molecular-weight.

Formulation specificities

- Sterilized.
- No paraben, alcohol, fragrance, animal origin ingredients, colouring and silicone.
- Non-animal tested.

User indications

- Topical application.
- Skin needling.
- Needle-free mesotherapy.
- Iontophoresis.
- Electroporation.
- Meso.

Meso protocol:

Depth: 1 to 3 mm.
Quantity per point: 0.03 to 0.10 cc.
Technique: Epidermic mesotherapy, Nappage, Point per point.
Needle: 30 G.

Can be mixed with:

25% to 50% F-HA+ (for expression wrinkles filling).

Injections remain under the full responsibility of the practitioner. The manufacturer or distributor can not be held liable for any kind and in any cases of damages caused to third parties, or adverse effects. The products are dully registered as topical use only.

About BTX system

Presentation:
The lift BTX system combines 3 molecules (Octapeptide, pentapeptide & low molecular hyaluronic acid) botulinum toxin-inspired concept. The octapeptide is an elongation of the famous hexapeptide ARGIRELINE®, it decreases neuronal excitability by SNARE complex destabilization. On the other side the pentapeptide also decreases neuronal excitability but by modulating acetylcholine (neurotransmitter) secretion. The combination of these 2 peptides guarantees the best results in the shortest time to reduce expression wrinkles caused by the contraction of muscles of facial expression, especially in the forehead and around the eyes. Peptides are a safer, cheaper, and milder alternative to Botulinum Toxin, topically targeting the same wrinkle-formation mechanism in a very different way. The peptides are combined to a high molecular weight cyclodextrin in order to provide an immediate and long lasting wrinkle reduction **(Figure 1: neuronal exocytosis and action mechanism of BOTOX®).**

Acetyl octapeptide-3 (Acetyl octapeptide-3):
Muscles responsible for the facial expression are contracted when they receive neurotransmitters released at the neuromuscular synapsis. An over- stimulation of the facial muscles, due to an excess of these chemical signals, leads to a greater skin strain. After the age of 30, first wrinkles start to appear as a consequence of such muscle contractions.
The study of the basic biochemical mechanism of anti-wrinkle activity led to the revolutionary hexa-peptide argireline®, which has taken the cosmetic world by storm. Continuous research on the treatment of such wrinkles has driven to *acetyl octapeptide-3*. This peptide is a new analogue of the N-terminal end of SNAP-25, that competes with the native protein for a position in the SNARE complex, essential for the muscle contraction **(Figure 2: action mechanism of acetyl octapeptide-3)**.

Pentapeptide-18 (Pentapeptide-18):
Expression wrinkles are a particular type linked to repeated muscular contraction and they usually appear as soon as the age of 30. Muscles are contracted when they receive acetylcholine released from a vesicle in the neuronal exocytosis. In order to fuse a vesicle with the cellular membrane, two events are required: the SNARE complex formation and the entry of calcium ions into the neuron. Pentapeptide-18 is a modified enkephalin that couples to the enkephalin receptor, outside of nerve cells. This association releases G protein subunits (α,β,γ) which close calcium channels avoiding vesicle fusion and consequently inhibiting acetylcholine release across the synapse **(Figure 3: action mechanism of pentapeptide-18)**. This process maintains the neuron in its resting state, attenuating muscle contraction and preventing the formation of lines and wrinkles.

Low-molecular-weight hyaluronic acid (Sodium hyaluronate):
Enables the skin to maintain skin homeostasis **(figure 4: hyaluronic acid structure)**. It reinforces tight junctions between keratinocytes **(figure 5: cellular junctions)**, thus limiting transepidermic water loss, thanks to its natural hygroscopic properties; it forms a "water reservoir" in the dermis. Also skin firmness is remarkably improved. Efficacy tests demonstrate that this specific grade of hyaluronic acid improves pro collagen I synthesis **(figure 6: cycle of collagen)**. The skin is firmer, better moisturized, and younger. **(Figure 7: hyaluronic acid low-molecular-weight action mechanism).**

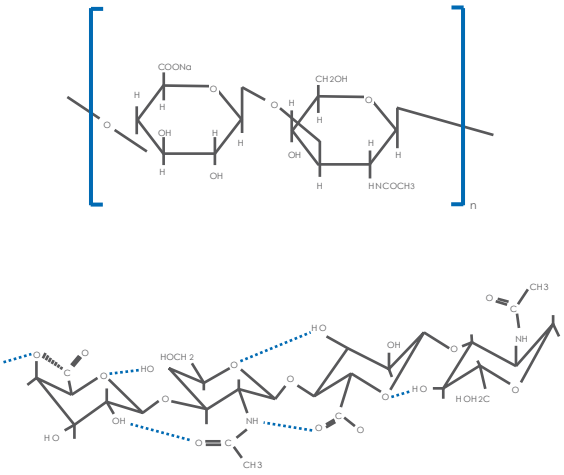


Figure 4: hyaluronic acid structure.

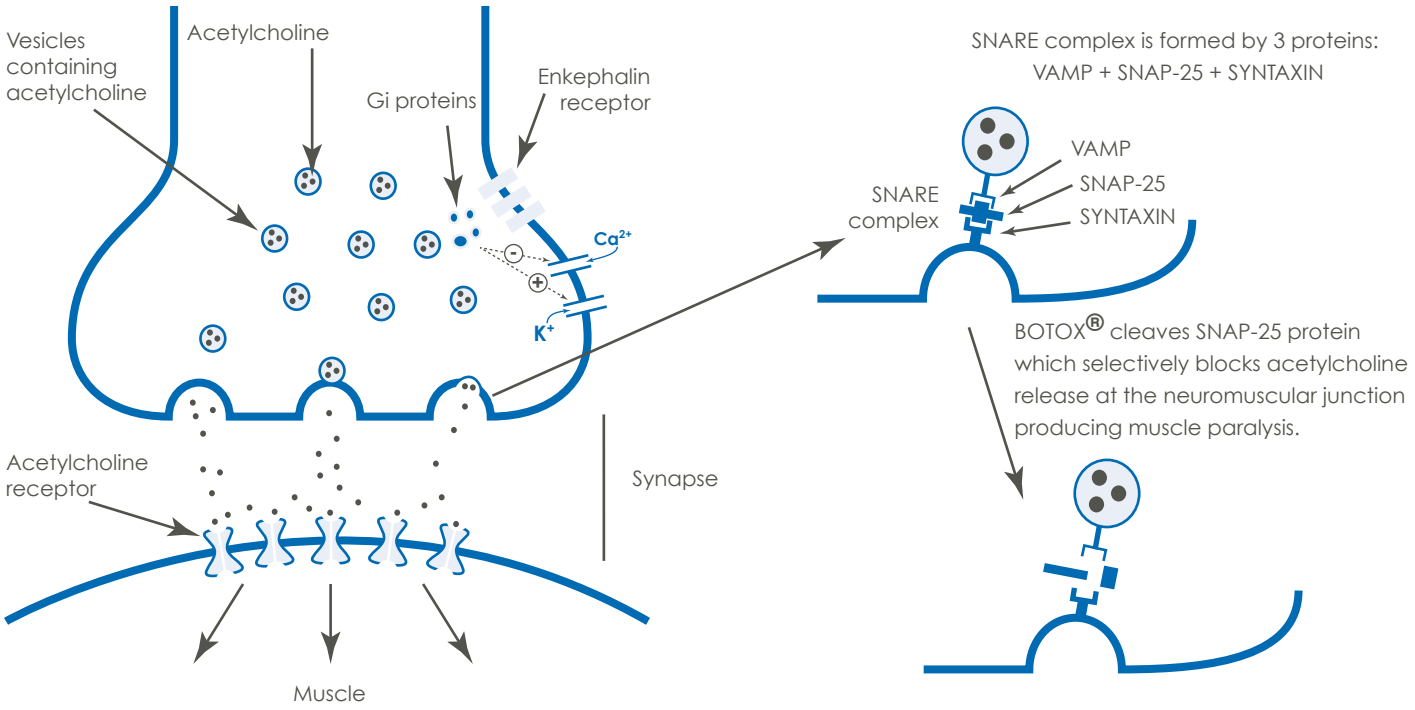


Figure 1: neuronal exocytosis and action mechanism of BOTOX.®

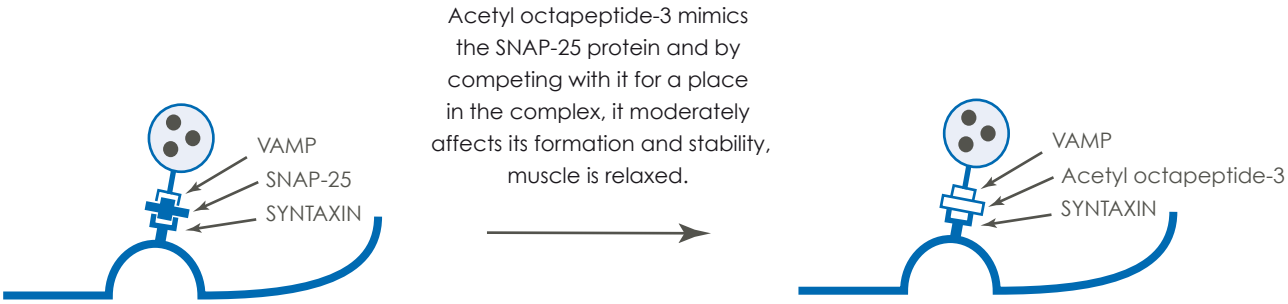


Figure 2: action mechanism of acetyl octapeptide-3.

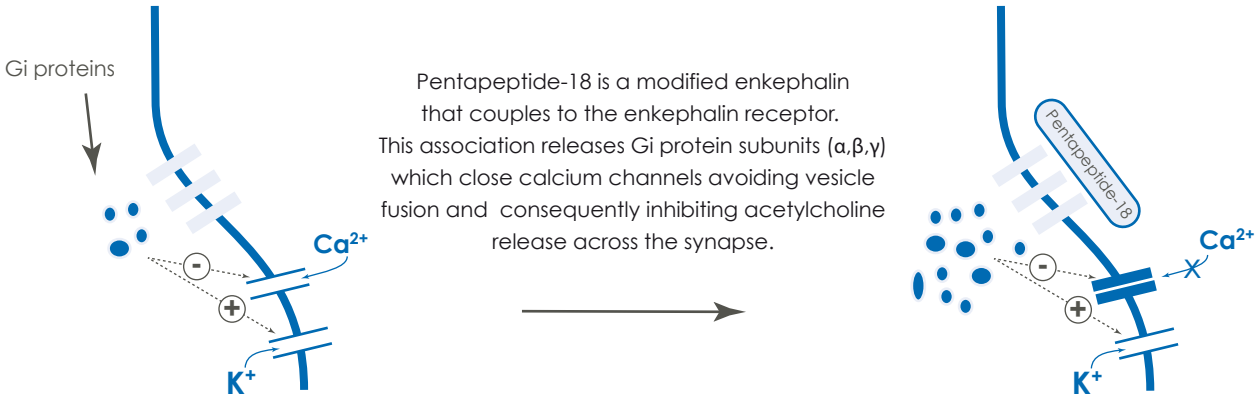
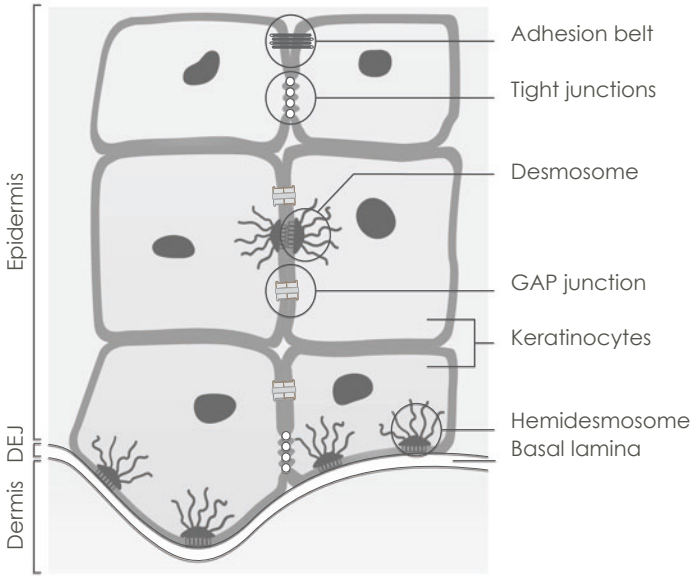


Figure 3: action mechanism of pentapeptide-18.



Multiproteic cell junctions in the epidermis

• Anchoring junctions bound cells one to another and enable the skin to assure rigidity and solidity. Desmosomes, adhesive junctions and hemi-desmosomes belong to this class.

• Gap junctions (or nexus) are responsible for intercellular communication. They are constituted of bound connexions, forming transmembrane channels that link the cytoplasm of two adjacent cells. Small molecules and ions may go through gap junctions, leading to metabolic and energy coupling of adjacent cells.

• Tight junctions (or zonulae occludentes) are in charge of cell waterproofness. They are mainly localized in the stratum granulosum. The main biological functions of tight junctions are:

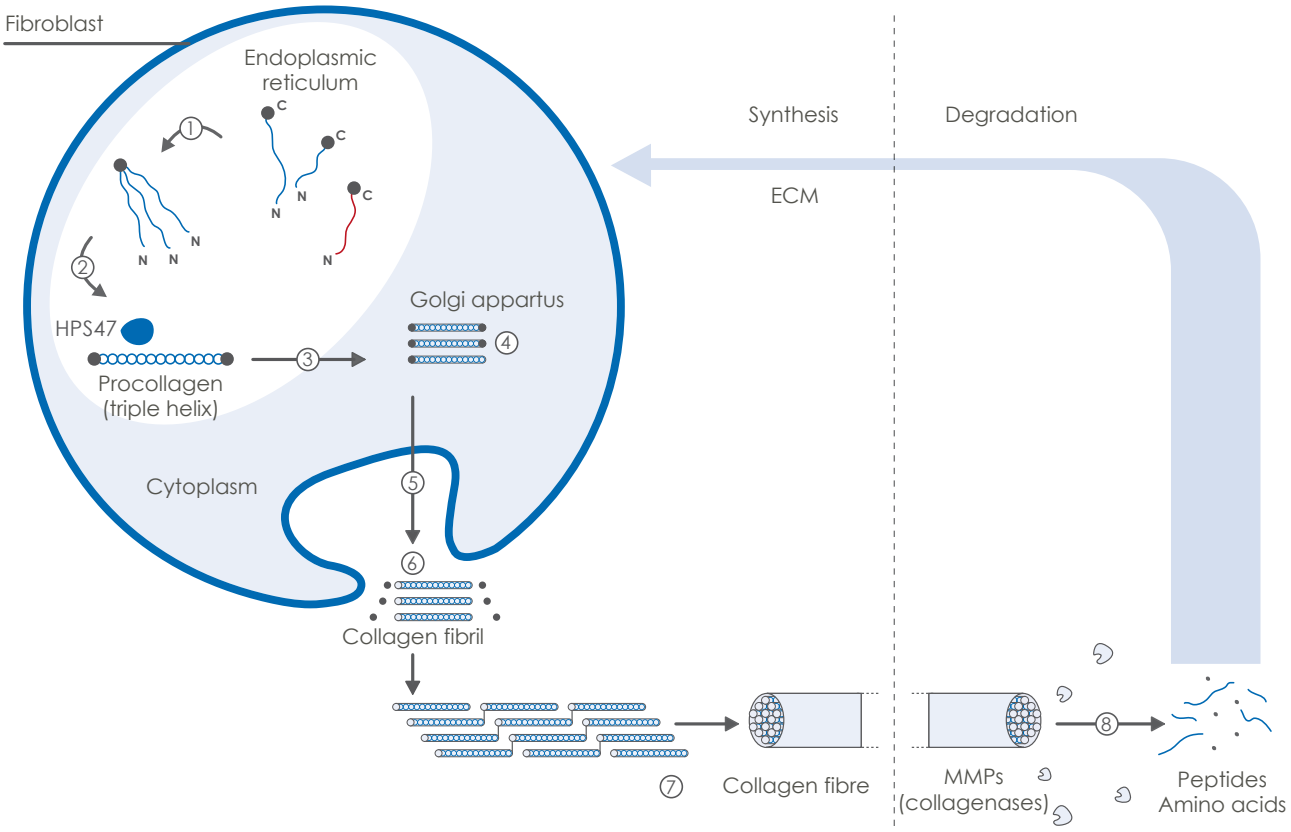
- Binding neighbouring cells, thus ensuring cell cohesion. They form a natural functional barrier (Tebbe et al., 2002).

- Regulating extracellular water flow and limiting transepidermic water loss.

- Jamming proteins and transmembrane lipid diffusion in the plasmic membrane, which contributes to the epithelial cell polarity.

Two constitutive proteins of these junctions have been described: ZO-1 and occludin. They are expressed in mature keratinocytes, in injured skin, and in vitro in differentiating keratinocytes (Pummi et al., 2001). A scientific study has evaluated the expression of these proteins during re- epithelisation and cell regeneration of the stratum corneum. Their role is also necessary in epidermis renewal as described by Malminen (2003). Tight junctions play a fundamental role in maintaining the integrity of the skin barrier, in epidermis hydration and in its organization. Intercellular junctions ensure mechanical and chemical cohesion between cells, but also cell communication. Ensuring these physiological activities helps to prevent skin ageing.

Figure 5: cellular junctions.



Collagen structure is made of three α polypeptidic chains of repeated units of Glycine, Proline and Hydroxyproline. Pro collagen α chains are synthesised (as every protein) in the endoplasmic reticulum (1). Oligosaccharides are added to the C-terminal pro peptide (2). Thus formed propeptides join to form trimmers that are linked covalently by disulfide bounds (3).

Procollagens are fold down and transported in the Golgi apparatus, where lateral association of the chains lead to fascicles (4). They are then secreted (5) and the propeptides are cut (6). Trimmers join into collagen fibrils that are then covalently bounded (7). These fibrils may then form bigger structures called collagen fibres.

Collagen is the support protein of the dermis. In aged skin, a decrease of collagen synthesis is observed, compared to younger skin (Varani et al, 2000). In parallel, an increase of degradation processes of collagen by specific Matrix Metallo Proteases (MMPs) occurs. Consequently, with time, elasticity and firmness of the skin decrease with age. The face contour blurs, eyelids sag, the skin weakens, gets thinner and less hydrated. Expression lines appear, wrinkles too. It is thus very important to improve collagen I synthesis, which represents almost 80% of dermis collagen.

Figure 6: cycle of collagen.

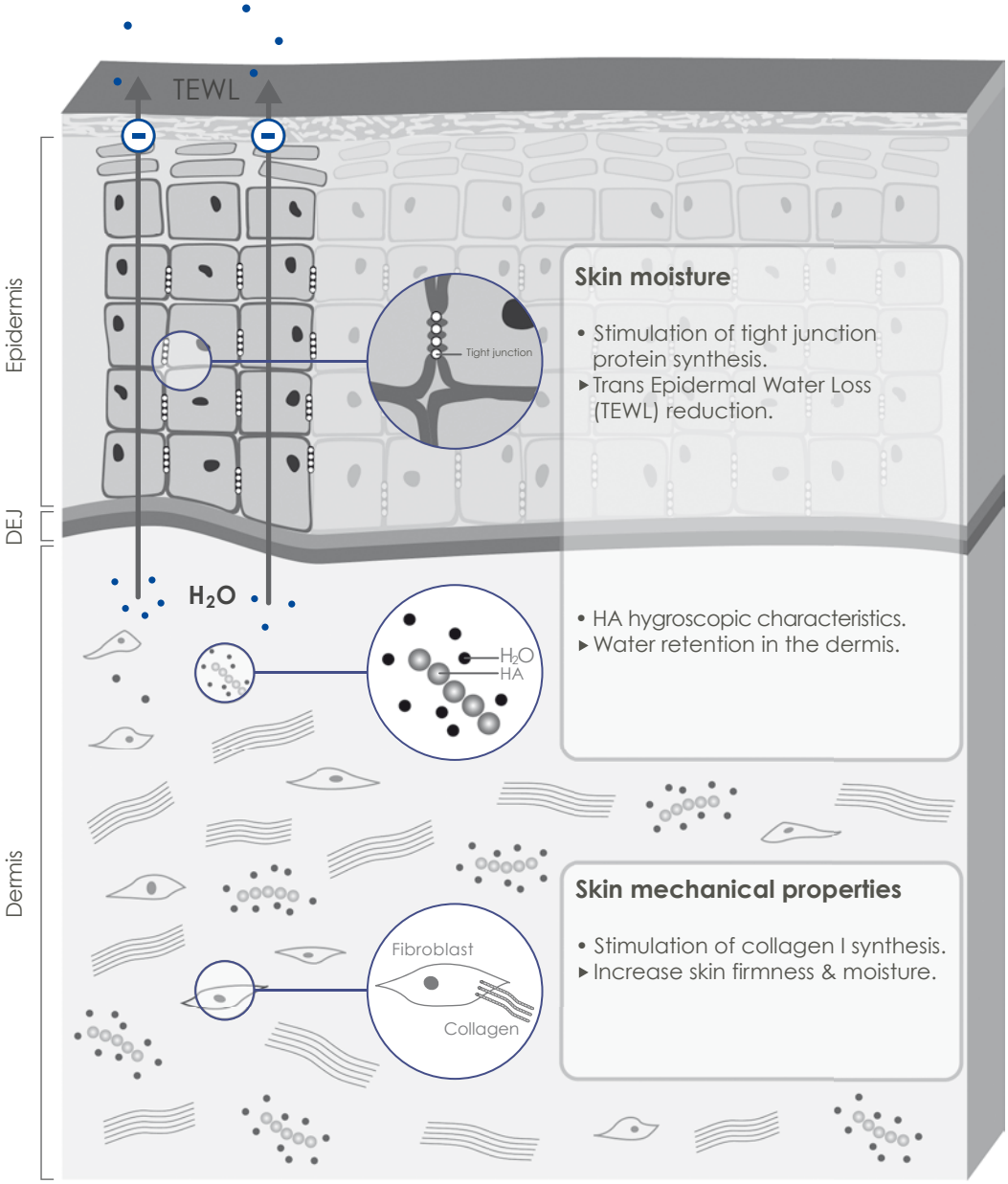


Figure 7: hyaluronic acid low-molecular-weight action mechanism.

Levels of activity of F-BTX system:

- Inhibits the SNARE complex formation by competing with the SNAP-25 natural protein.
- Inhibits the release of neurotransmitters.
- Close calcium channels avoiding vesicle fusion and consequently inhibiting acetylcholine release across the synapse.
- Long term reduction of expression wrinkles.
- Cytostimulation and oxygenation (the products contain oxygenation factor).
- Improves cellular moisture.
- Improves skin moisture.
- Reduce transepidermic water loss.
- Produce skin tightening, reduce wrinkles and fine lines thanks to collagen I synthesis stimulation.
- Reorganise the dermal matrix.

Clinical results:

Inhibition of snare complex formation.

To evaluate the antagonistic competitive efficacy of the peptide patterned after the SNAP-25 N-terminal domain compared to the native SNAP-25 (positive control), acetyl octapeptide-3 capacity to assemble with syntaxin and synaptobrevin forming the SNARE complex was measured. Heat and the consequent thermal decomposition was used as the negative control. Acetyl octapeptide-3 blocks the formation of the SNARE complex. The lower the formation of the SNARE complex in vitro, the higher is the efficacy of the anti-wrinkle active.

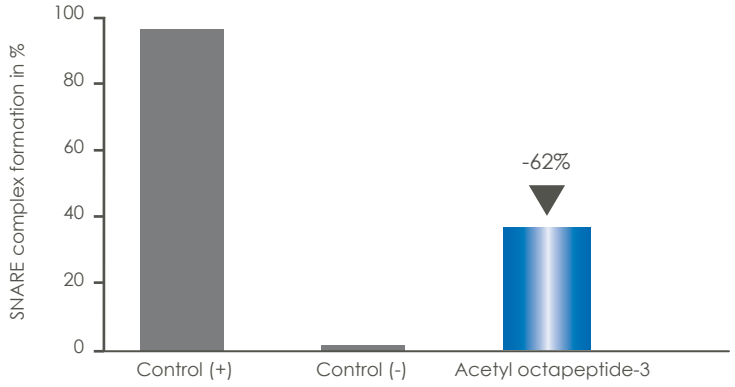


Figure 4: inhibition of snare complex formation by acetyl octapeptide-3.

Modulation of catecholamine release in chromaffin cells.

Inhibition in the release of catecholamines was determined by monitoring the neurotransmitters Adrenaline and Noradrenaline, by liquid scintillation counting. Chromaffin cells were incubated with these neurotransmitters and acetyl octapeptide-3 (100 µM). The significant modulation at µM concentrations is a clear indicator of the potent anti-wrinkle activity of acetyl octapeptide-3.

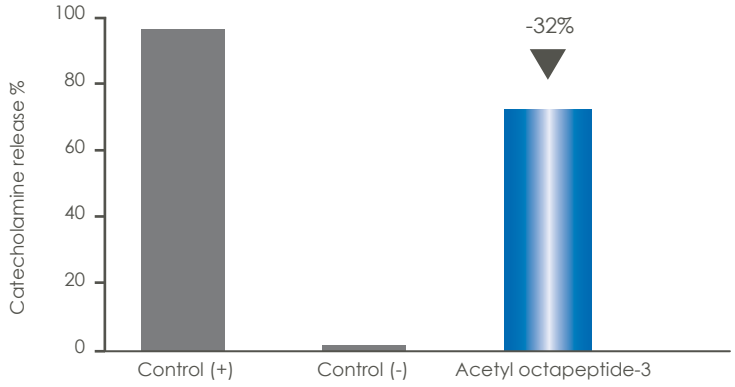


Figure 5: modulation of catecholamine release in chromaffin cells by acetyl octapeptide-3.

Modulation of glutamate release in a neuron cell culture by botox-like peptides compared to Botulinum toxin A.
Glutamate is the most excitatory abundant neurotransmitter in the nervous system and its release is used as a validated assay to determine the release of acetylcholine. The release of glutamate in a primary cell culture of neurons is measured in order to compare the in vitro activities of the anti expression-wrinkle peptides pentapeptide-18, Argireline®, pentapeptide-18 + acetyl octapeptide-3 compared to Botulinum toxin A. The independent mechanisms of pentapeptide-18 + acetyl octapeptide-3 show together a higher inhibitory potential in glutamate release, because of their complementary effects. As the inhibition of the glutamate release is directly dose-dependant.

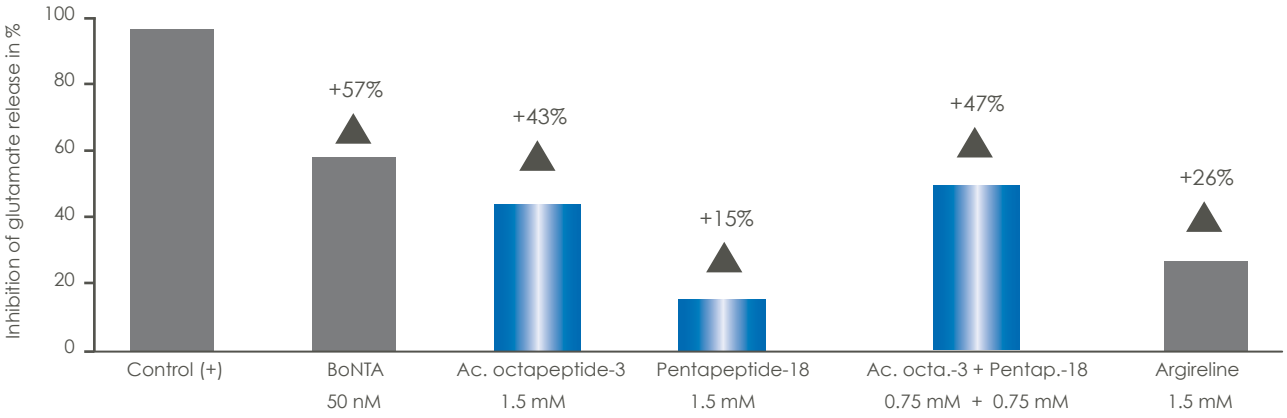


Figure 6: modulation of glutamate release in a neuron cell culture.

In vivo anti-wrinkle efficacy of acetyl octapeptide-3.
Skin topography analysis were performed to measure the effectiveness of a cream containing 10% acetyl octapeptide-3 solution, applied twice a day. Silicon imprints were obtained from around the eyes of 17 women volunteers pre-test and after the 28 days treatment. Analyses of the imprints were performed by confocal profilometry. The maximum reduction value of wrinkle depth was 63% and average value was 35%, the same test performed with Argireline produced an average value of 27%.

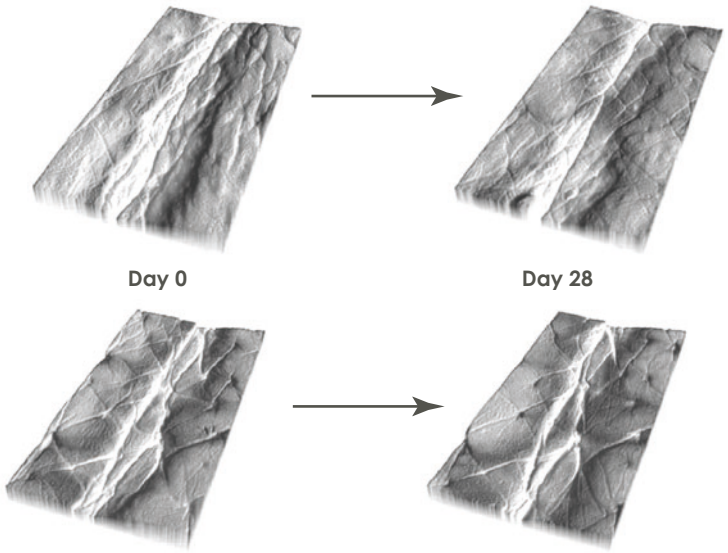


Figure 7: anti-wrinkles efficacy of acetyl-octapeptide-3.

Improvement of skin moisture (in vivo).

A study was conducted to assess the skin moisture as compared to the untreated skin. Following a one-week conditioning period to standardize the skin condition, 33 female voluntary panelists arrived at the testing lab. Two test sites were defined on the panelists' forearms. Baseline measurements were taken in duplicate with the Corneometer. Following baseline measurement, 0.2 ml of the product was applied to the assigned site. Corneometric readings at 15 minutes, 8 hours, and 24 hours were measured. As shown in Graph, the product offers a significant increase of moisture: 30% improvement after 15 minutes and most important 14% at both 8 and 24 hours after product application.

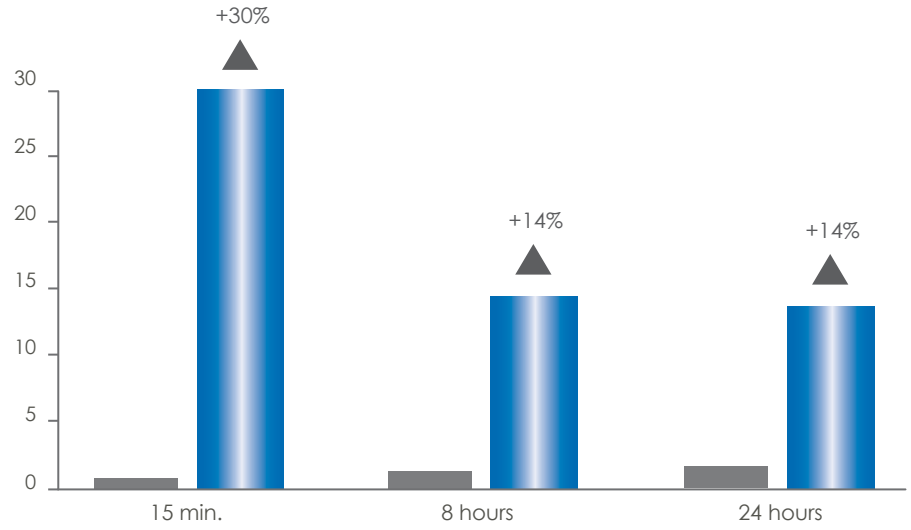


Figure 6: low-molecular-weight hyaluronic acid moisturizing test.

Improvement of tight junctions (in vitro).

A culture of keratinocytes was treated with low-molecular-weight hyaluronic acid, and then ZO1 and Occludin proteins have been isolated by electrophoresis and quantified. This experiment has been processed on normal human keratinocytes (NHK) stemming from plastic surgery. The result was an improvement of the protein synthesis 29% for ZO1 and 39% of Occludin.

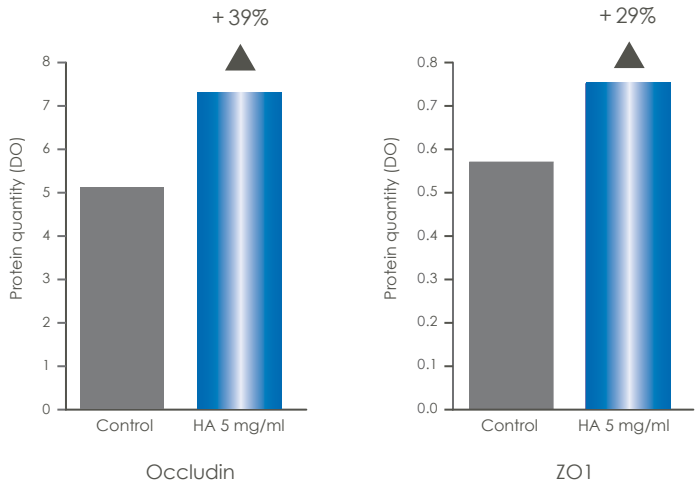


Figure 7: low-molecular-weight hyaluronic acid effect on tight junctions proteins.

Collagen synthesis stimulation (in vitro).

Collagen I is the most abundant protein of the dermis. It is synthesised by fibroblasts and is involved in skin firmness. The test aims to prove that low-molecular-weight hyaluronic acid increases collagen I synthesis by measuring type I pro-collagen quantity (PIP) after application of low-molecular-weight hyaluronic acid 5 mg/ml. The test has been processed on aged human fibroblasts stemming from plastic surgery. Dosage of the proteins present in the cell pellets after treatment of the cells with the product was processed. It is expressed in µg of cell proteins and related to PIP dosage for each cell well. The stimulation percentage was calculated as follows, with the quantitative values of PIP related to proteins: ([produced PIP] – [control PIP] x 100. The result was an improvement of collagen I synthesis of more than 21%.

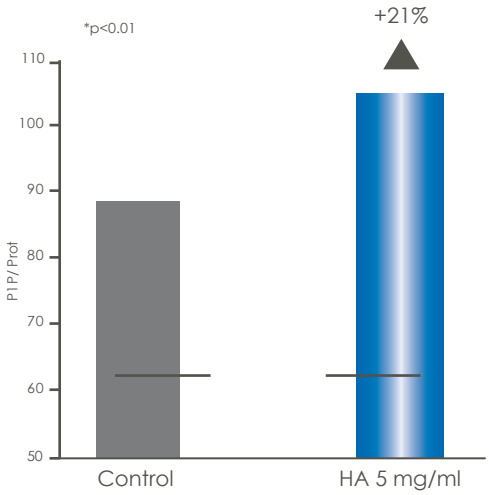


Figure 8: low-molecular-weight hyaluronic acid collagen stimulation effect.