[F-LIFT+ FACE]

Product identity

F-LIFT+ FACE formula is the ultimate anti-ageing and firming treatment. Each vial is containing only the pure active ingredients, without any preservatives or other chemicals. This formula is a totally breakthrough in skin rejuvenation. Peptides and growth factors are the main ingredient of this formula with various effects as cystostimulation, free radicals blocker, anti-glycation, anti-wrinkles, firming, collagen synthesis booster and skin lightening. It´s complemented to increase the skin tightening with Carcinine and hyaluronic acid also providing moisture and skin volume. Thanks to this exclusive product skin ageing can be effectively prevent and a natural rejuvenation achieved.

Benefits

- Prevents skin ageing.
- Neutralizes free radicals.
- Reduces oxydation process.
- Reduces wrinkles & fine lines.
- Stimulates collagen I synthetis.
- Firms the skin and restores the skin structure.
- Moisturizes.
- Improves skin softness
- Sooths irritated and damaged skin, reduces redness.
- Reduces skin hyperpigmentation and improves skin lightening.
- Replaces or complements hyaluronic acid micro-injections.

Active ingredients

- Hyaluronic acid 0,25%
- N-acetyl-glucosamine-6-phosphate 0,25%
- Hexapeptide-10 1%
- Carcinine 0,25%
- CG-βFGF 0,20%
- CG-IGF1 0,25%
- CG-TRX 0,20%
- CG-EDP3 0,25%
- CG-TGP2 0,25%

Formulation specificities

- Sterilized by filtration.
- 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 4 mm.
Quantity per point: 0.03 to 0.10 cc.
Technique: Nappage, Papule, Point per point.
Needle: 30 G.

Can be mixed with:

Use the product pure.

About LIFT+ FACE system

Presentation:

The LIFT+ FACE system is an extreme solution for skin firming, skin tigthening and to achieve a perfect complexion. The formula contains a blend of innovative ingredients in particular HA, NAG6P, peptides and growth factors:

Hyaluronic acid low molecular weight: Our low-molecular-weight hyaluronic acid 50.000 - 150.000 Daltons is strictly identical to the molecules present in the skin. This specific molecular weight enables it to enter the skin and act directly in the epidermis and even in the dermis in order to regulate moisture and to increase skin firmness. It globally acts to reduce transepidermic water loss (TEWL) phenomenon, which consists in water evaporation at the surface of the skin. As demonstrated further, it also reinforce the skin cellular tight junctions, increases water retention in the dermis & stimulates collagen I synthesis.

N-acetyl-glucosamine-6-phosphate: A concentrated and natural NAG6P as unique source of skin building block, which feeds the cutaneous cells, stimulates their regeneration and supports the production of Hyaluronic acid and other GAGs at the epidermic and dermic level. A unique technology for deep rejuvenating effect.

Hexapeptide-10 (peptide): This hexapeptide mimics a sequence of Laminin, promoting cell adhesion as well as cell proliferation. This pro-firmness ingredient acts in both keratinocytes and fibroblasts. It increases the production of laminin-5, integrin and hemidesmosomes, thus strengthening the dermal-epidermal junction.

Carcinine 2HCL (peptide): This exclusive active ingredient is a strong anti-oxydant and anti-inflammatory.
Preventive action : counteracts the protein oxydative cross-linking, particularly due to fatty acid hydroperoxydes.
Repairing action : reduces and detoxifies the membrane hydroperoxides (reverse effect).

CG-bFGF (growth factor): Anti-ageing and anti wrinkle effect by generating new skin cells and inducing synthesis of collagen and elastin. Accelerates also wound healing and repair.

CG-IGF1(growth factor): Treat the appearance of lines and wrinkles by increasing cell proliferation and inducing synthesis of collagen and elastin.

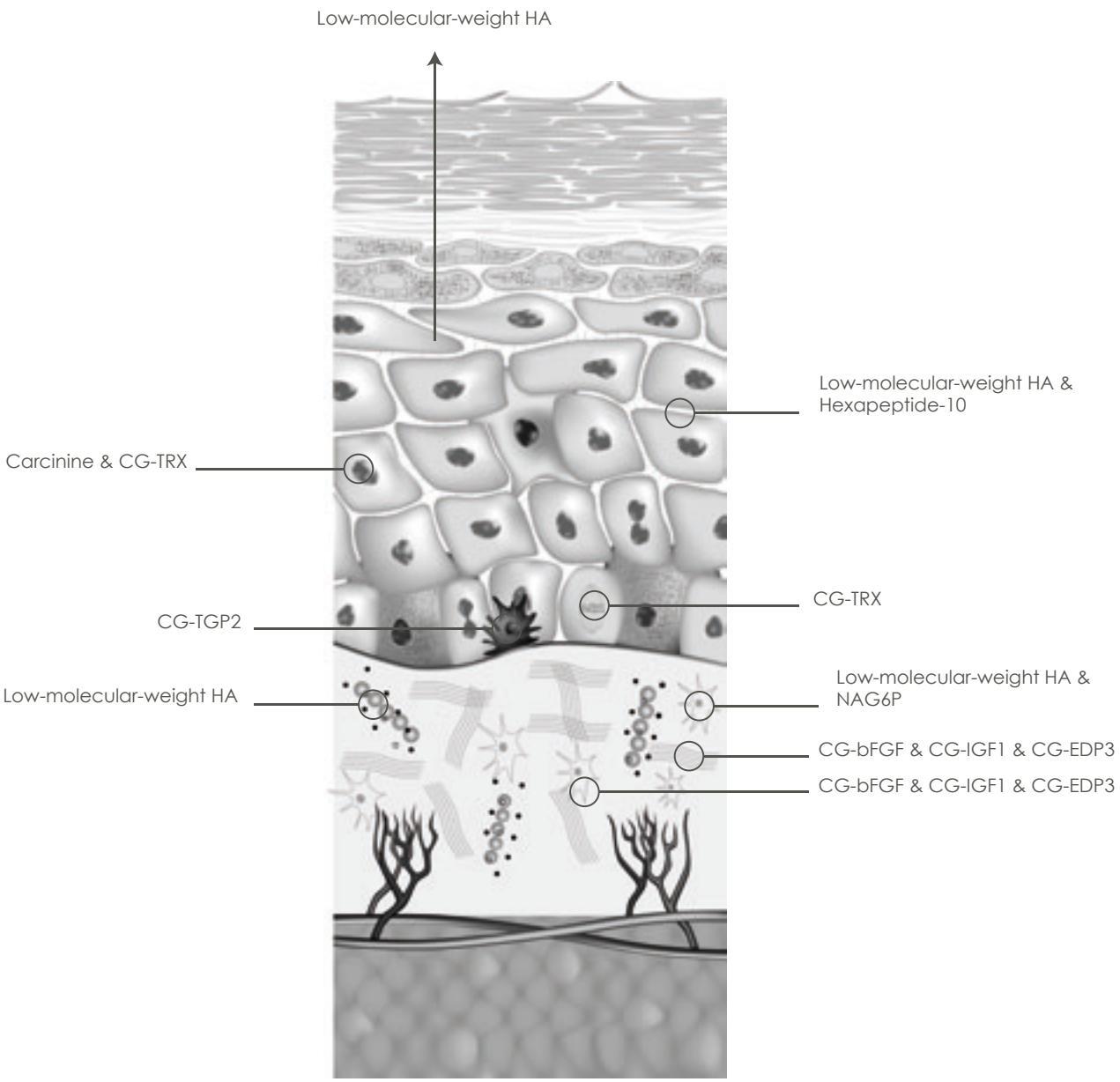
CG-TRX (growth factor): Strong anti-oxidant reducing free radicals, visibly provide a luminous and up lifted complexion.

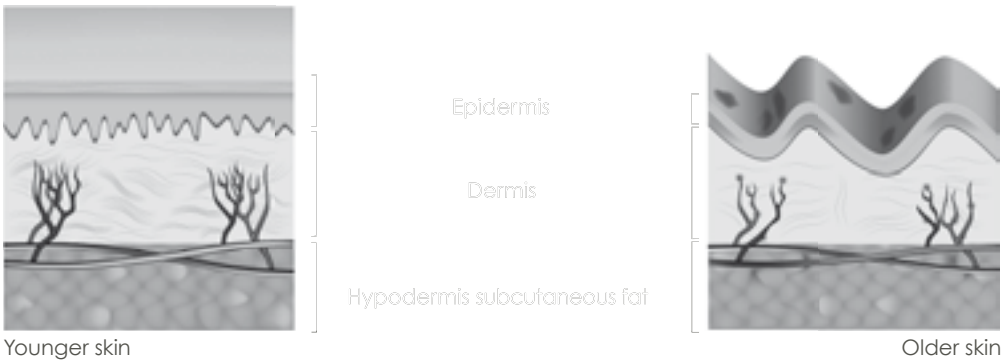
CG-EDP3 (biomimetic peptide): anti-ageing biomimetic peptide up-regulating cell growth and migration. Increases hyaluronic acid expression by 3 folds and fibronectin expression by 1.3 fold.

CG-TGP2 (biomimetic peptide): anti-pigmentation biomimetic peptide decreasing the expression level of TRP1, Tyrosinase and TRP2. Inhibit melanosome transfer to keratinocyte. Restrain the proliferation of activated T cell and inhibit expression of TH1 type "proinflammatory cytokine".

Focus on free radicals (Figure 1: inflammation process):
Free radicals are atoms or molecules with one ore more single, non-paired electrons. Because they are missing one or more electrons free radicals are highly unstable. They tend to collide with other, stable molecules and then steal an electron in order to stabilise themselves. This destabilises the molecules that they have collided with leaving them without an electron. Radicals of oxygen, called reactive oxygen species (ROS), are unstable and react the quickest with other molecules. ROS are produced as natural by products of the oxidative cell metabolism in our body. Exposure to UV-light leads to additional oxygen radicals. ROS are toxic for our cells because they lead to the formation of cytokines and inflammatory reactions destroying essential cellular components such as lipids, DNA or down regulating the collagen synthesis.

Focus on collagen breakdown (Figure 2: cycle of collagen):
Fibrillar collagen and elastic fibres are the protein components of the dermis that impart strength and resilience to the skin. During normal aging, the skin becomes thinner, looser and less elastic. This loss of firmness is principally the consequence of a profound atrophy of the dermal protein structure. With advanced age, the fibroblast cells produce less collagen and elastin and more enzymes (elastase) that specifically breakdown these structural proteins. This production of elastase is due to free radicals and the formation of cytokines and interleukins that they induce. These cytokines act on a receptor at the surface of the fibroblast that true a chain of reactions activate the transcription factor of elastase and down regulates the expression of collagen. Free radicals, inflammation process and collagen breakdown are closely linked.





Action mechanism of LIFT+ FACE system

By reacting to environmental stress, the skin plays the important role of protection against harmful effects. As a wide and complex organ, it presents a whole range of biological mechanisms made to answer precisely to external stimuli such as brutal temperature changes or UV exposure. One of these physiological mechanisms is inflammation. Unfortunately, this may cause anaesthetic and uncomfortable consequences. Inflammatory mediators and arachidonic acid cascade are the main elements in the inflammation process, in particular when sun exposure leads to sunburn. They lead to Leucotriene and Prostaglandine release, indirectly responsible for the appearance of erythema.

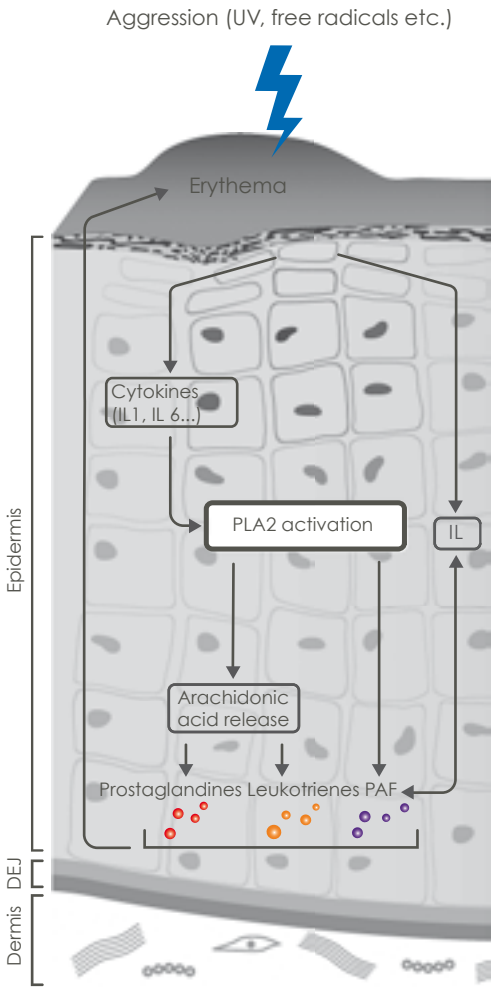
Focus on two inflammation mediators: cytokines and lipidic mediators. Cytokines are soluble proteins or glycoproteins, synthesised, stored and carried by immune cells (lymphocytes, monocytes and activated macrophages) as well as skin cells (keratinocytes and fibroblasts). Cytokines are called interleukines (IL) when released by lymphocytes T, monocytes and macrophages. Cytokines may also be named in relation with their function: interferons (INF), growth and differentiation factors, colony-stimulating factors. Pro-inflammatory and anti-inflammatory cytokines exist.

LIFT+ FACE system has been proved to protect the cellular membrane of keratinocytes avoiding that they produce immune modulating molecules, such as lipidic mediators or cytokines.

Inflammatory lipidic mediators produced by keratinocytes regroup the platelet activation factor (PAF), lysophosphatidic acid, arachidonic acid-derived metabolites and ceramids.

Pro-inflammatory cytokines, such as: Interleukines (1, 6, 8, 12, 15, 18), TNF- α, TGF- β, Interferon- β, Granulocyte macrophage colony stimulatory factors. These cytokines maintain, spread and amplify the inflammatory reaction.

This results on a reduction of skin erythema, lipid, DNA and collagen destruction.



Inflammatory Reaction

Inflammatory reaction is a physiological answer of our body to exogenous (UV, heat, cold, acids, bacteria) or endogenous stimuli (immune reaction). The four clinical symptoms that characterise inflammation are redness, oedema, heat and pain. Inflammatory reaction occurs through three complex steps: Initiation phase, Amplification phase, and Repairing phase. Many cell types and chemical mediators are implied in these biological reactions.

Cells and mediators

Initiation

Specific: Lymphocytes T antibodies (immunoglobulins).
Non-specific: Neutrophiles, eosinophiles, monocytes and macrophages, complement, Hageman factor.

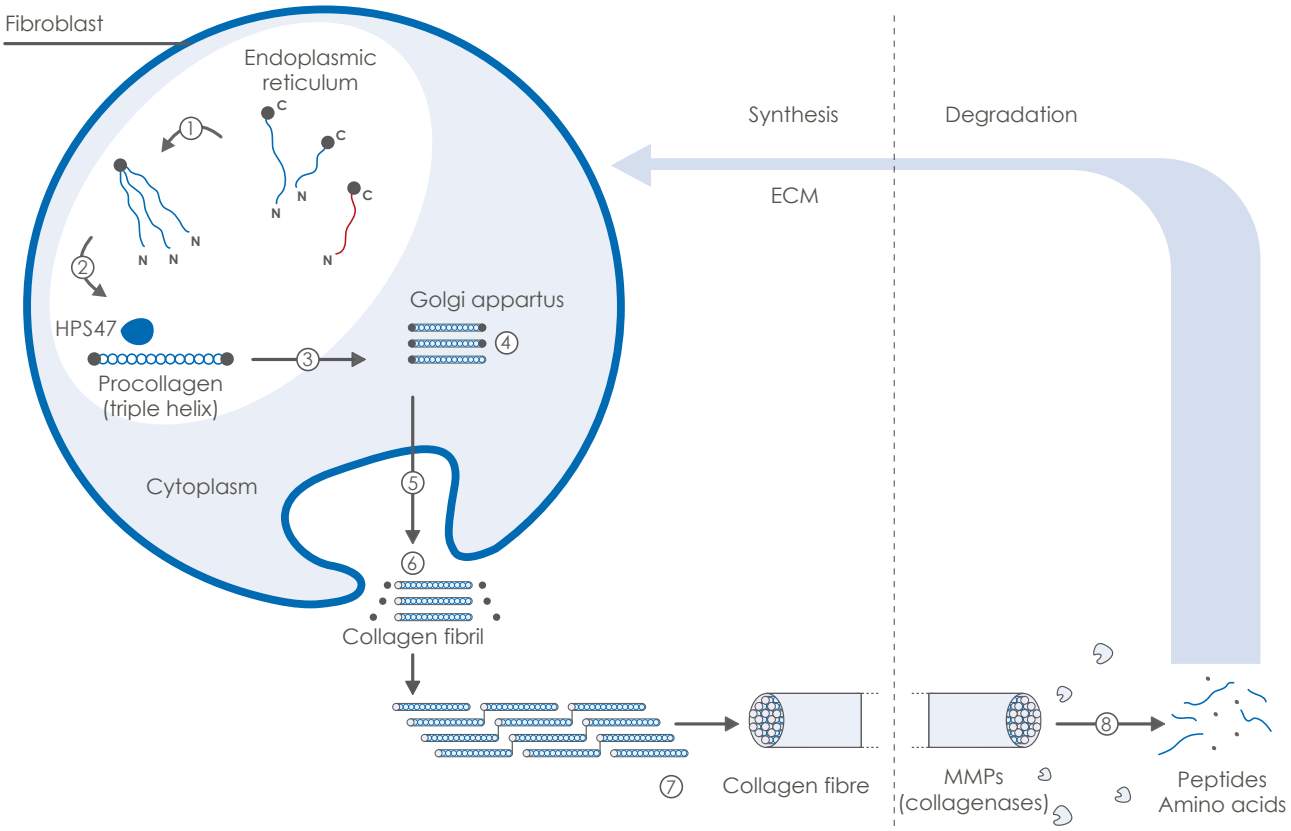
Amplification

Complement, lipidic mediators (arachidonic acid products, platelet activation factor PAF), histamin, bradykinin, serotonin, coagulation cascade, cytokines (IL-1, IL-6, IL-8, IL-11, TNF-α, INF-α, INF-β, chemokines, growth factors), lysosome enzymes.

Repair

Neutrophiles, eosinophiles, macrophages, lymphocytes T, perforins, ROS.

Figure 1: inflammation process.



Collagen structure is made of three α polypeptidic chains of repeated units of Glycine, Proline and Hydroxyproline. Procollagen α chains are synthesised (as every protein) in the endoplasmic reticulum (1). Oligosaccharides are added to the C-terminal propeptide (2). Thus formed propeptides join to form trimers that are linked covalently by disulphide 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). Trimers 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 2: cycle of collagen.

[HYALURONIC ACID LOW MOLECULAR WEIGHT]

Name: Hyaluronic acid
Effect: Anti-ageing & anti-wrinkles
Our low-molecular-weight hyaluronic acid (certified Ecocert) 50.000 - 150.000 Daltons is strictly identical to the molecules present in the skin. This specific molecular weight enables it to enter the skin and act directly in the epidermis and even in the dermis in order to regulate moisture and to increase skin firmness. It globally acts to reduce transepidermic water loss (TEWL) phenomenon, which consists in water evaporation at the surface of the skin. The skin is thus less moisturised, loses its flexibility, tonicity and softness.

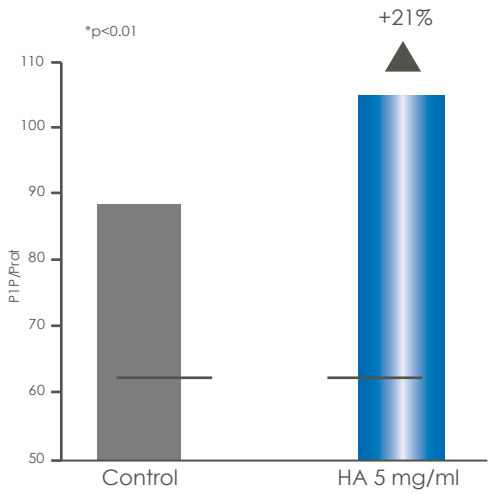
Reinforcement of skin cellular tight junctions
The epidermis is formed by cohesive keratinocytes, living a life cycle of 28 days, while they differentiate from the basal towards the surface. Cell cohesion is essential to regulate this mechanism and to ensure cell renewal and differentiation. Cells are thus related one to another by cell junctions. Different types of junctions exist with multiple but specific roles: sealing, signal communication, chemical transmission. Among them, tight junctions are essential for skin barrier integrity, ensuring cell cohesion. They enable keratinocytes to form a natural functional barrier in the stratum granulosum, leading to water flow regulation and TEWL limitation. Hyaluronic acid stimulates the expression of ZO1 and Occludin proteins that are constitutive proteins of tight junctions. This improves cell cohesion and the barrier function of the skin.

Increase water retention the dermis & stimulation of collagen I synthesis
The dermis is mainly constituted of fibroblasts and the extracellular matrix (ECM), where collagen, elastin and glycoaminoglycans such as hyaluronic acid may be found. Hyaluronic acid is of paramount importance in skin moisturising and collagen synthesis by fibroblasts, necessary for skin support. Skin ageing causes an increase in their degradation and a decrease in their synthesis. The consequence is a loss of suppleness and flexibility, leading to wrinkle formation and dehydration.

Source: Biofermentation
Vectorisation: low molecular weight
Dosis in F-LIFT+ FACE: 0.25%

Clinical trials

Collagen synthesis stimulation by low-molecular-weight hyaluronic acid (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%.

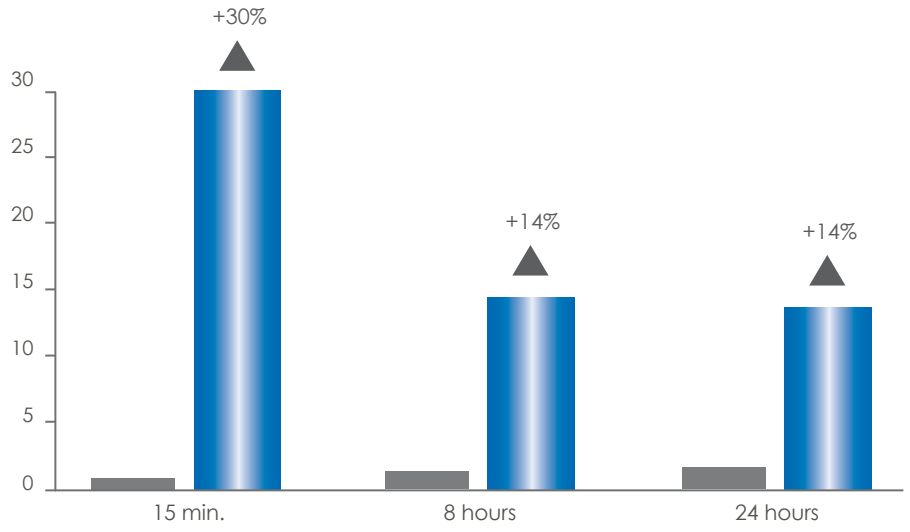


Low-molecular-weight hyaluronic acid collagen stimulation effect.

[HYALURONIC ACID LOW MOLECULAR WEIGHT]

Improvement of skin moisture by low-molecular-weight hyaluronic acid (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.



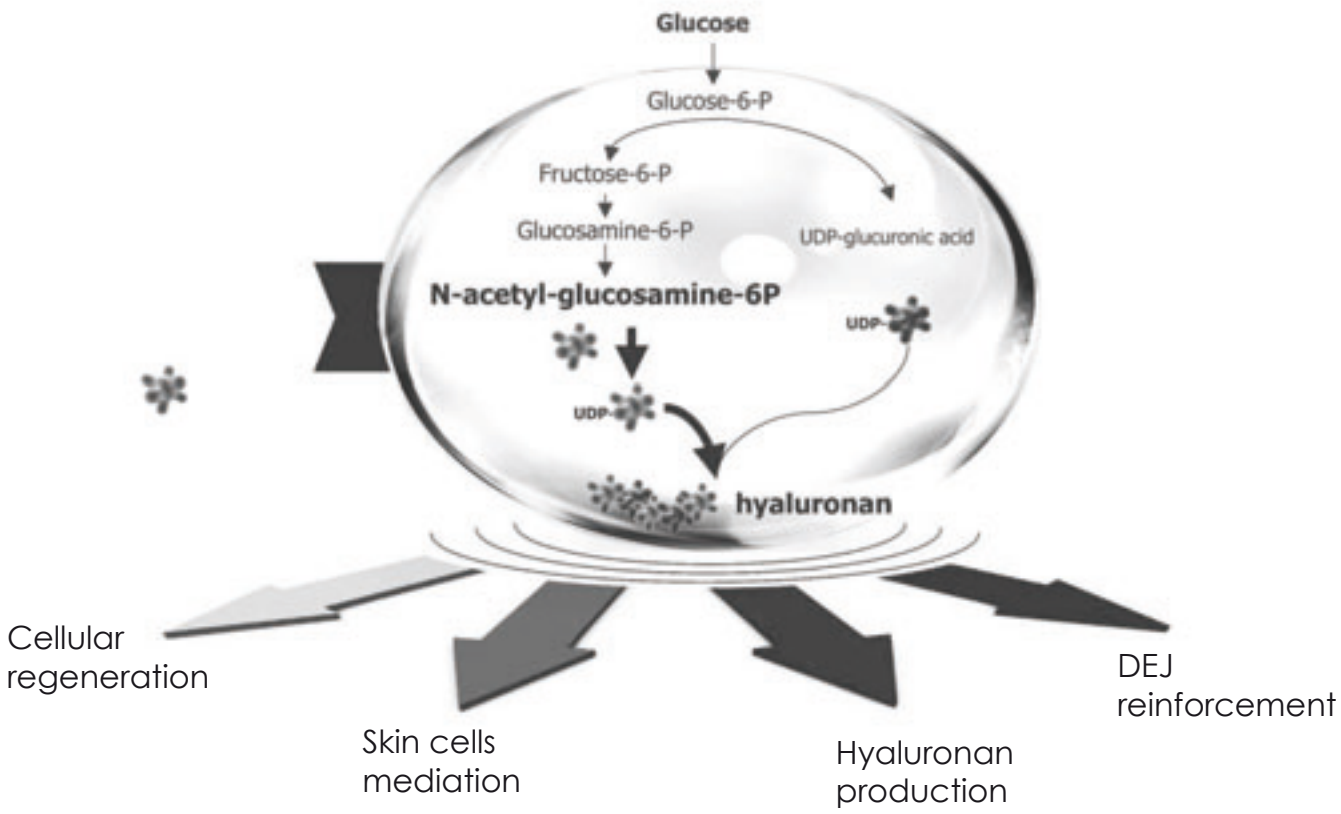
Low-molecular-weight hyaluronic acid moisturizing test.

[NAG6P]

Name: N-acetyl-glucosamine-6-phosphate
Effect: Molecular pro-filler
NAG6P is the result of two years of biotechnology research to enable the green and efficient synthesis of the ultimate active intermediate used by our skin cells to synthesize hyaluronan and reinforce skin intercellular communication: N-acetyl-glucosamine-6-Phosphate.

NAG6P represents a really new conception in cosmetics : the 'molecular fuelling concept'. As an high energised intermediate, it directly feeds skin cells with the natural building metabolite they require to enhance their production of GAGs and hyaluronic acid (+282%). Furthermore, it energizes skin remodelling by strengthening DEJ within less than 10 days, and it boosts skin cells communication (epidermo-dermis mediation) leading to fibroblast regeneration (120%), thus promoting a global three dimensional rejuvenating effect.

Source: Biotechnologies
Vectorisation: -
Dosis in F-LIFT+ FACE: 0.25%

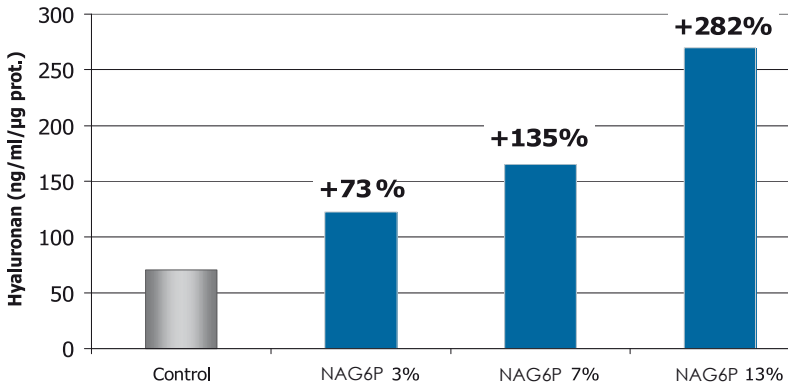


[NAG6P]

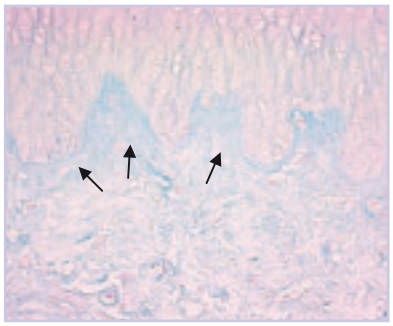
Clinical trials

Filler effect

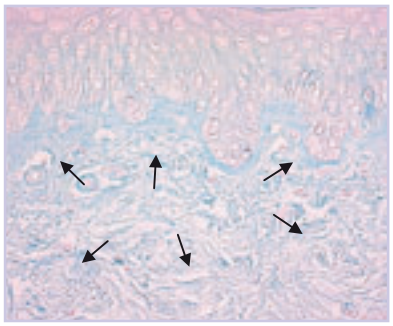
IN VITRO: Hyaluronic acid synthesis improved up to +282% in 48h00 in topical use.



EX VIVO: Stimulation of GAG production in papillar dermis after 6 days.

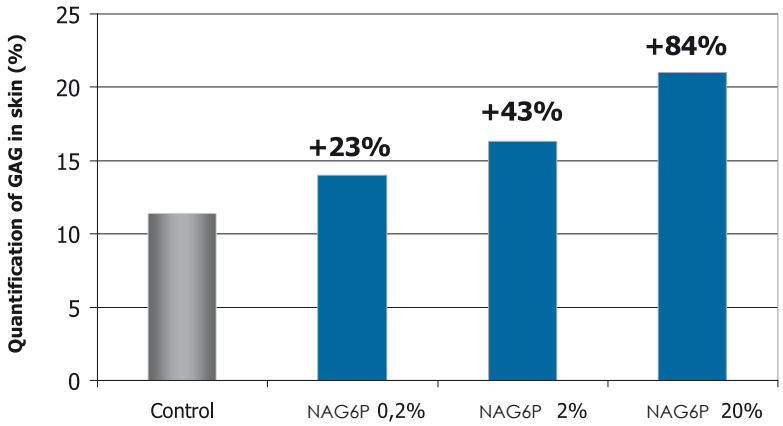


Untreated skin - control
Low amounts of GAG (blue colour) mainly located around the DEJ



Skin treated with NAP6G
Clear amounts of GAG well distributed in the entire papillar dermis

EX VIVO: Stimulation of GAG production in papillar dermis after 10 days.

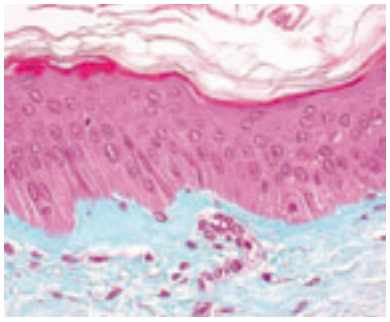


[NAG6P]

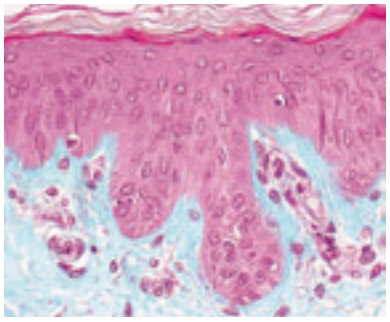
Clinical trials

Firming and smoothing effect

EX VIVO: Reorganization and restructuring of dermis epidermis jucntion after 10 days on humna skin.



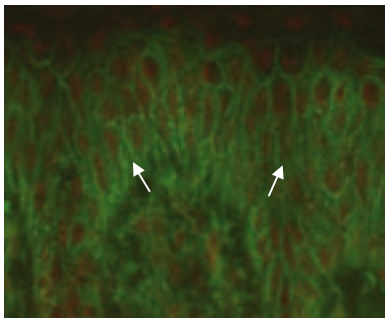
Untreated skin - control
Good epidermis structure
but weak dermis epidermis junction.



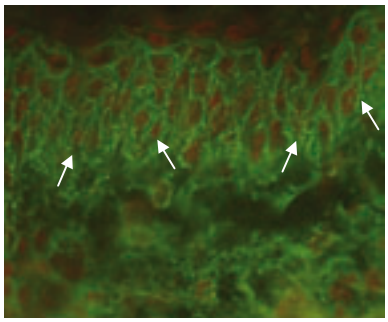
Skin treated with NAP6G 0.2%
Good epidermis structure and
excellent dermis epidermis junction.

Regeneration effect

EX VIVO: Expression of CD44 receptors (hyaluronan receptor) in the basal layer after 10 days on humna skin.

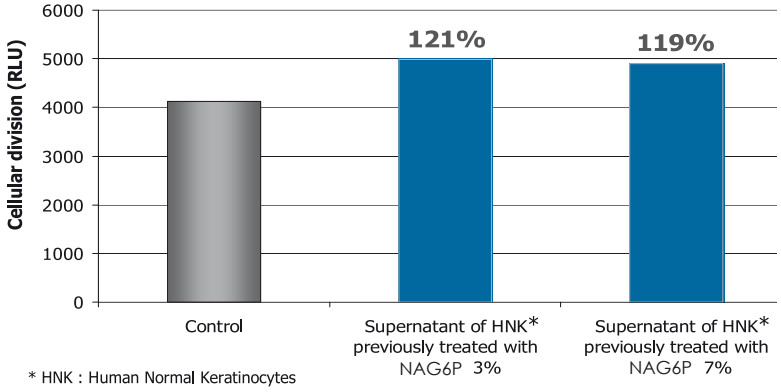


Untreated skin - control
Clear expression of CD44 receptors
at the level of the basal layer.



Skin treated with NAP6G 0.2%
Very clear expression of CD44 receptors
at the level of the basal layer.

EX VIVO: Mediation of cell communication, stimulation of fibroblasts division induced by keratinocytes up to 120% in 48h00.



* HNK : Human Normal Keratinocytes

[HEXAPEPTIDE-10]

Name: Hexapeptide-10
Effect: Firming
The study of the mechanisms of skin aging has traditionally overlooked an important area: the dermo epidermal junction (DEJ). This is the layer responsible for supporting the epidermis and for the communication between epidermal and dermal cells. The DEJ is physically a basement membrane that separates the skin cells in the epidermis from the extracellular matrix (ECM) which lies below, in the dermis. This membrane is composed by two layers, the basal lamina, in contact with the cells, and the underlying reticular lamina, in contact with the ECM. The basal lamina is rich in collagen type IV, proteoglycans and the glycoproteins entactin and laminin. These molecules provide a structural network and bioadhesive properties for cell attachment.
Laminin is a glycoprotein of about 850 kDa and it is, after collagen, the most abundant protein in the ECM. However, while Collagen performs exclusively a structural role in the skin, Laminin is involved in functionalisation and activation of cells, in processes such as cell proliferation, migration and adhesion. These mechanisms are necessary to keep the normal balance of the skin and are essential for processes as important as wound healing, for instance.
Laminin only exists in basement membranes. It is composed of three very long polypeptide chains (alpha, beta and gamma) arranged in the shape of an assymetric cross and held together by disulfide bonds. The three chains exist as different subtypes which results in twelve different isoforms for laminin, of which the best well- studied is Laminin-1.
Keratinocytes recognise the binding domains on Laminin, particularly Laminin-5, by using their own integrin receptors, transmembrane proteins located on specific junction points called hemidesmosomes.

Hexapeptide-10 consists in a sequence from the alpha chain of Laminin. This peptide retains many of the chracteristics of the native protein, and promotes cell adhesion and proliferation. Certain features of the DEJ are altered by the aging process, such as the anchoring ability of keratinocytes, probably due to deficiencies in the expression of integrins as we age.
Laminin-5 synthesis has also been proved to decrease in aged skin. This causes a loss of contact between dermis and epidermis, and results in the skin losing elasticity and becoming saggy. The cohesion between dermis and epidermis is essential to maintain skin balance because it enables the transport of oxygen, nutrients and waste, contributing to the health of the epidermis. This work will show that a synthetic hexapeptide from Laminin-1 is able to restore the skin's normal function by promoting synthesis of Laminin-5, stimulating keratinocyte and fibroblast proliferation, inducing a redensifying effect on the dermis, and an improvement in skin elasticity, compactness, tonicity and smoothness.

- Hexapeptide-10 improves cell adhesion by enhancing synthesis of Laminin-5.
- Adhesion of cells to the basement membrane and among themselves provides firmness to the skin.
- Increased contact between skin cells ensures correct nourishment and health.
- Hexapeptide-10 induces a significant increase in the dermis density, improving skin compactness.

Source: Biotechnologies
Vectorisation: -
Dosis in F-LIFT+ FACE: 1%

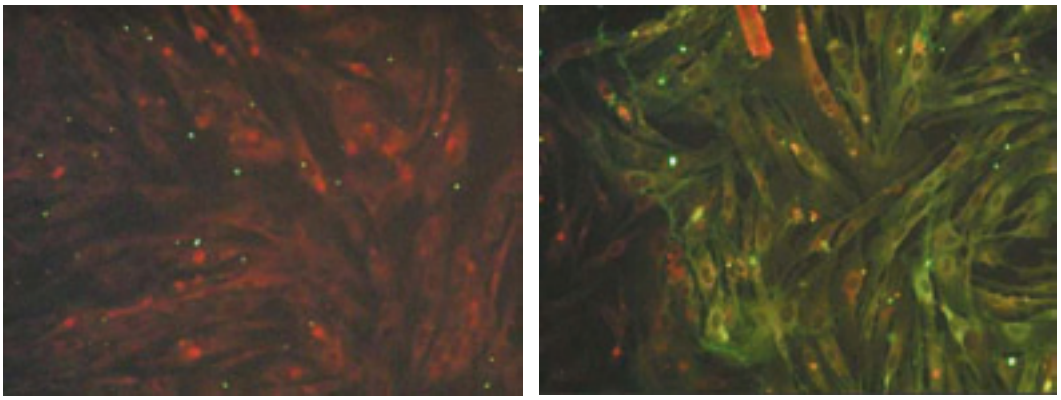
Clinical trials
In vitro
Stimulation of Laminin-5 production (I)
Immunostaining studies have been carried out in human fibroblasts (the natural producers of Laminin) in order to ascertain if Hexapeptide-10 is able to enhance the expression of Laminin-5.

The test uses a primary (monoclonal) antibody that binds to Laminin-5, and a secondary antibody (polyclonal) that binds to the complex between protein and primary antibody. The secondary antibody is coupled to a fluorescent compound (FITC – Fluorescein Isothiocyanate).

FITC is illuminated with filtered light at 495 nm (absorption wavelength) and the light emitted by the dye is detected at 528 nm (emission wavelength).

Trypsinised fibroblasts were incubated for 72 hours in microplates with 0.05 mg/mL Hexapeptide-10, Minimal Essential Medium-Na-Piruvate and 5% FCS. Cells were then fixed and incubated with the primary antibody and then with the secondary antibody coupled to the dye (FITC). For the immunofluorescence analysis we used an Olympus fluorescence microscope (20x magnification).

[HEXAPEPTIDE-10]



Immunofluorescence – Laminin-5 expression in untreated human fibroblasts

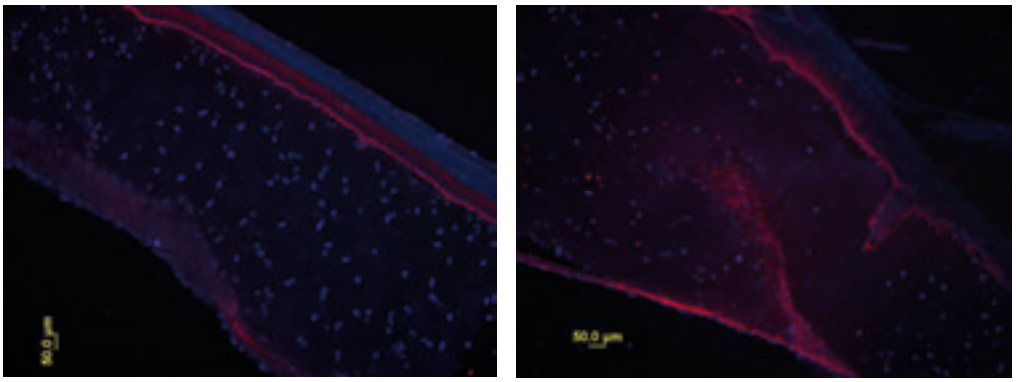
Immunofluorescence – Laminin-5 expression in treated human fibroblasts

Figure 1. Expression of Laminin-5

Stimulation of Laminin-5 production (II)

The full thickness skin models exhibit in vivo-like morphological, metabolical, and growth characteristics which are uniform and highly reproducible. These skin-like tissues consists of organized basal, spinous, granular and cornified epidermal layers analogous to those found in vivo (1).

Human skin tissue models were used to monitor the levels of Laminin-5. EpidermFT full thickness skin model (supplied by Mattek Corporation, Ashland, MA, USA) consists of normal, human-derived epidermal keratinocytes (NHEK) and normal, human-derived dermal fibroblasts (NHFB) which have been cultured to form a multilayered, highly differentiated model of the human dermis and epidermis.



Control

Hexapeptide-10 0,005%

Figure 2 . Red Immunofluorescent stain for Laminin-5 in organotypic cultures

Fluorescent quantification by image analysis demonstrates that laminin-5 is expressed 20% more in treated tissues than controls (figure 3.)

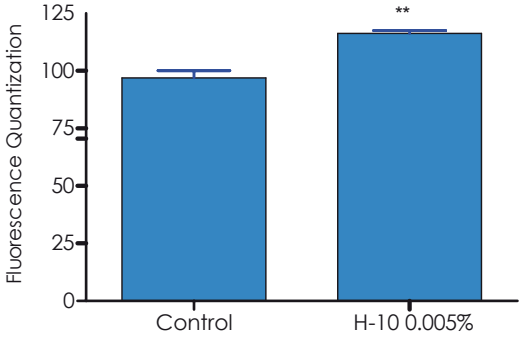
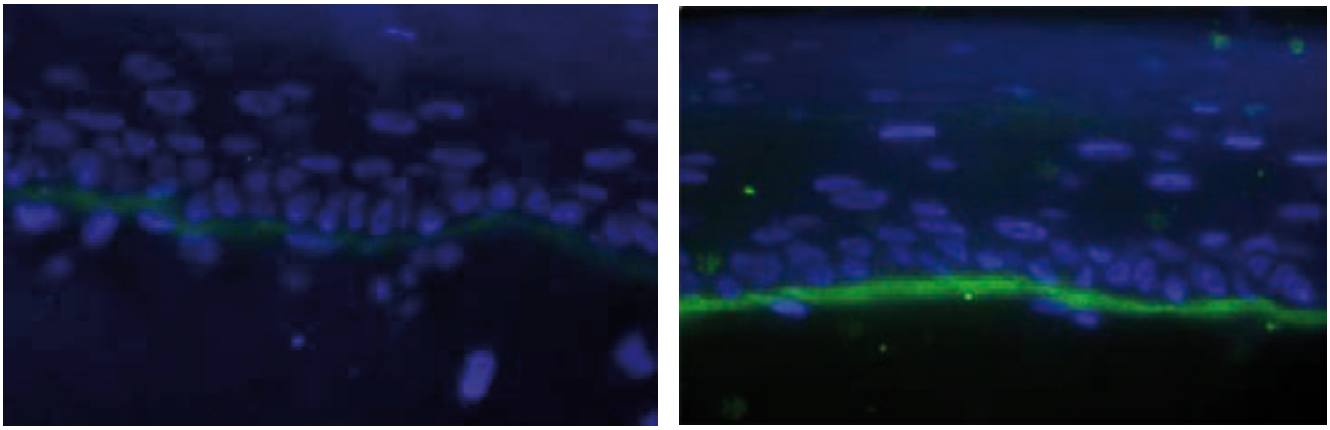


Figure 3. Fluorescence quantization of Laminin-5 expression in skin models untreated (control) or treated with Hexapeptide-10 0.005% (**P<0.01).

[HEXAPEPTIDE-10]

Stimulation of α 6-integrin production (I)

By immunohistochemistry, we evaluated the synthesis α6-Integrin, which is synthesized by keratinocytes and mediates their adhesion to the basement membrane. Hexapeptide-10 has shown to increase integrin synthesis in the basement membrane zone of the organotypic cultures (Figure 4). Figure 5 shows the fluorescence quantification calculated by image analysis with Metamorph software. Integrin expression is 75% higher in Hexapeptide-10 treated tissues than in controls.



Control Hexapeptide-10 0,005%

Figure 4. Green Immunofluorescent stain for 6 a-integrin in organotypic cultures

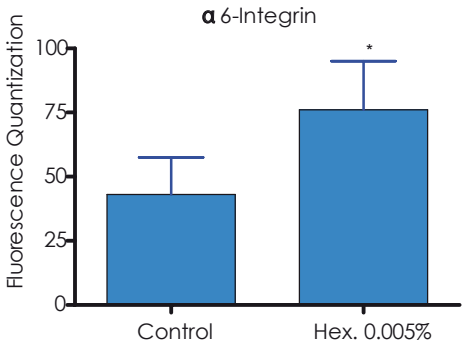
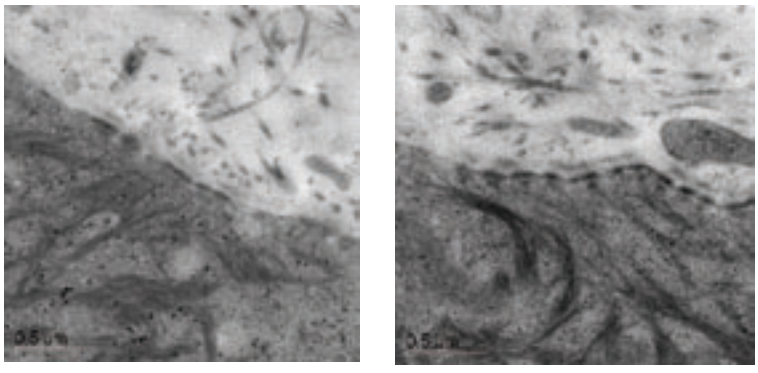


Figure 5. Fluorescence quantification of 6 a-integrin expression in skin models untreated (control) or treate with Hexapeptide-10 0.005% (*P<0.05).

Stimulation of hemidesmosome formation (I)

Both proteins, α 6-integrin and Laminin-5, form a cell structure called hemidesmosome, that can be seen by transmission electron microscopy as electron- dense plaques. Hexapeptide-10 at 0.005% has proved to increase the number of hemidesmosomes (Figure 6), thus increasing cohesion between dermis and epidermis.



Control Hexapeptide-10 0,005%

Figure 6. transmission electron microscopy observation of skin models sections

[HEXAPEPTIDE-10]

Evaluation of the dermis density
A panel of 20 female volunteers aged 55 to 64 (average 62) were treated with Hexapeptide-10 Solution twice daily during 54 days. The volunteers applied a placebo cream on one side of the face and the active cream on the other.
Measurements were made using the high frequency echograph Dermascan C® 2D. The measurement principle is that of the echograph: an ultrasound beam is emitted by piezo-electric ceramics. This beam is partially reflected by the interface separating two mediums of different ultrasound impedance. At the interface between two types of tissue, the wave will be refracted, and part of the wave will be reflected back and detected by the apparatus. How much is reflected depends on the densities of the respective tissues. The ultrasound used is equipped with a 20 MHz probe, which is applied directly to the skin. A contact gel provides homogeneous diffusion of the signal.
This method allows the bi-dimensional visualization of the skin on the epidermis and dermis. It is also possible to measure skin thickness (epidermis and dermis) and evaluate dermis density. Therefore, the effect of an anti-aging product can be evaluated. The accuracy of this method is estimated to be 2%.

An image analysis software is used to calculate dermis density. An increase in the dermis density characterises a redensifying effect of the tested product.

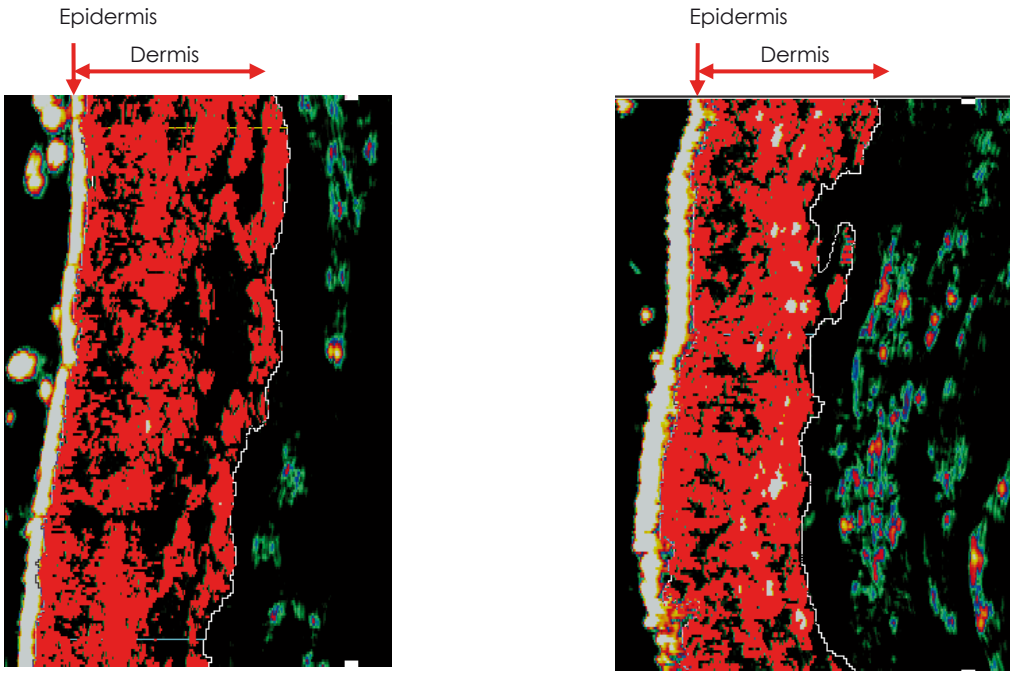


Figure 7. Example of obtained image for volunteer 11

After 54 days, the cream containing Hexapeptide-10 had induced a long-term redensifying effect of 19%, compared to the measure at Day 0. The placebo did not induce a significant redensifying effect.

[CARCININE]

Name: Carcinine
Effect: Antioxydant, antiglication, metabolism stimulator
Besides intrinsic aging, the skin is under the constant aggression of oxidative entities (solar radiations, pollution, physical stress, etc.). The resulting oxidative stress can affect the structure of the cutaneous tissue and the metabolic activity of its composing cells such as fibroblasts and keratinocytes. Since these factors are essential for the quality of the skin, carcinine is a peptidic compound which is able to protect the skin components such as the collagen from these aggressions and to maintain the metabolic activities of the exposed cells.
Treatment with Carcinine will both prevent and repair the daily aggressions-induced damages, allowing the skin to remain healthy, firm and beautiful. Alistin acts in three different, non-exclusive, ways for a maximal efficiency:
1) Anti-oxidation / anti-stress
2) Anti-glycation
3) Metabolism stimulation
Hence, carcinine protects and/or reduces the noxious effects of an exposure to oxidative stress that can eventually lead to severe damage as shown below:

Cellular & Skin level
1) Accumulation of oxidative forms
Protein alterations (including structural proteins) DNA mutation
Structural collapse, loss of elasticity, fine lines
Tissue inflammation
Less efficient dermis tightening activity
2) Protein glycation (including collagen)
Homeostasis loss
3) Slackening of cell metabolism
Dehydration

Source: Nature-identical compound obtained from the decarboxylation of carnosine
Vectorisation: -
Dosis in F-LIFT+ FACE: 0.25%

Clinical trials

Cell detoxification
Peroxidase-like activity (Babizhayev et al., 1994 - TI_0239)
Reduction of acid forms threatening the integrity of cells' membrane
Faster DNA recovery after stress (Exsymol - DO_0751)
Global scavenger + free radical-induced damages repair (Exsymol, DO_1044)

Skin structural proteins protection (Collagen)
Anti-glycation activity (Exsymol - DO_1133)
Combination of 3 defense mechanisms: competition, detoxification and reverse-glycation (Exsymol - DO_1133)

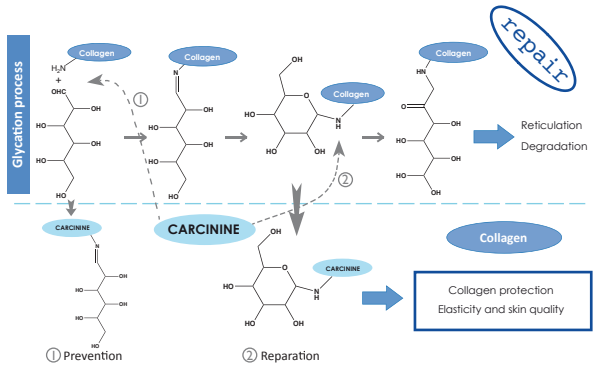
Metabolic protection and stimulation
Control of pro-inflammatory cytokine production (Exsymol - DO_1157)
Increase of sirutun expression (Fréchet et al., 2010 - A3_1295)
Increase of collagen production rate (Fréchet et al., 2010 - A3_1295)

[CARCININE]

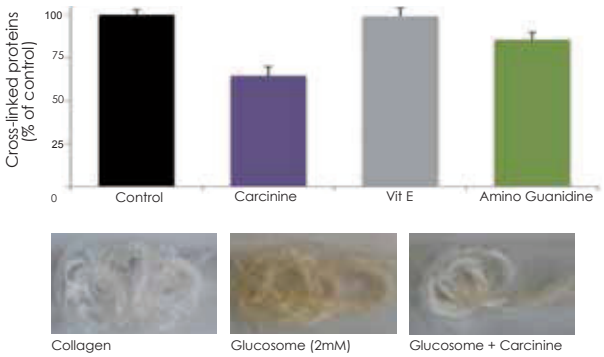
Carcinine preventing and repairing cutaneous damage effect

Carcinine for anti-glycation

Carcinine protects the collagen and other proteins from the glycation processes at two different levels:
1 Prevention: by glucose scavenging.
2 Reparation: by substituting itself to the collagen in a transglycation process.

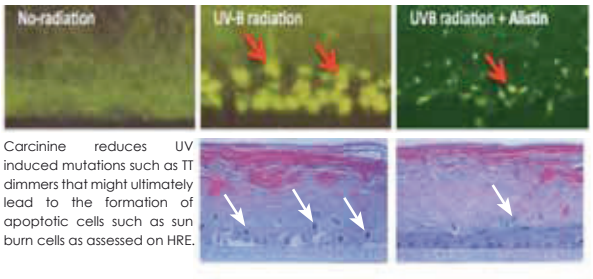


Hence, Carcinine prevents the protein from cross-linking, while other anti-oxidants such as vitamin E fail at it. Carcinine is even more potent than aminoguanidine, a reference in anti-glycation. Furthermore, the final products of the reaction are neither toxic nor mutagenic.



The skin preserves its structure and elasticity

Carcinine protects from UV-induced DNA damage

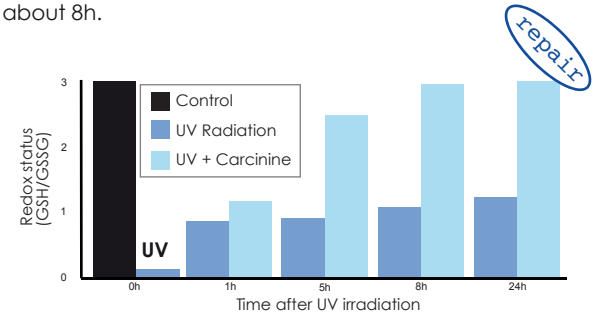


Carcinine reduces UV induced mutations such as TT dimmers that might ultimately lead to the formation of apoptotic cells such as sun burn cells as assessed on HRE.

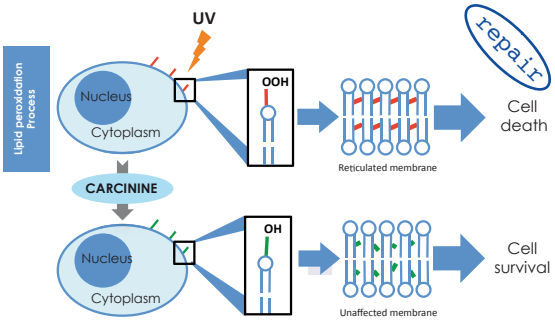
Carcinine protects the DNA from UV-induced damage and mutation. Carcinine stimulates the production of DNA-protecting proteins, hence decreasing the number of apoptotic cells.

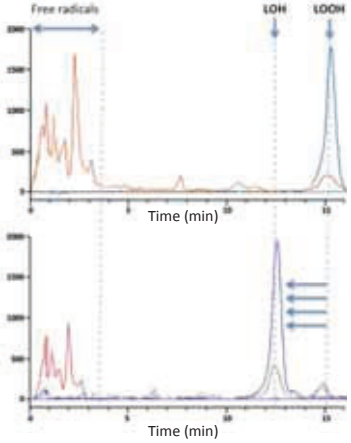
Carcinine a unique anti-oxidant

UV radiation can induce damage that can be monitored by measuring the cells redox status. The skin can slowly recover by itself from UV irradiation. However, even after 24h, the self healing process still was not complete. Treatment with Carcinine led to a full recovery in just about 8h.



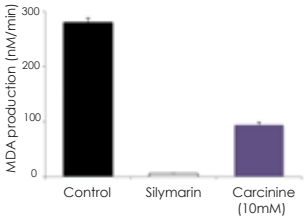
Carcinine provides a fast and reliable protection against oxidative stress-induced damage as measured above.





Carcinine reduces the noxious LOOH (lipid peroxide) into harmless alcohol LOH, preventing the protein degradation into toxic free radicals as assessed by HPLC. This anti-oxidative effect is unique and is not shared by other anti-oxidants such as Vitamin E.

Carcinine's anti-oxidative properties are also due to its scavenging power 200 as shown by its ability to reduce MDA (a toxic byproduct of oxidative stress) production.



The skin is protected, healthier.

[CARCININE]

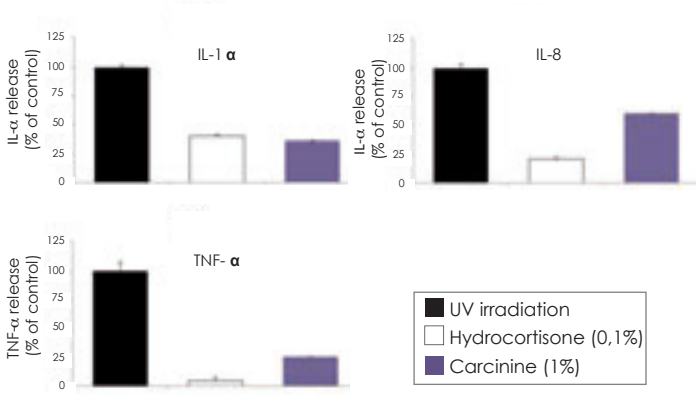
Carcinin positive effects on skin cells' metabolism and function.

Carcinine reduces skin inflammation

Aggressions can lead to skin inflammation. Carcinine, when applied on human reconstituted epidermis, reduces the secretion of pro-inflammatory cytokines such as TNF-α, IL-1α and IL-8.

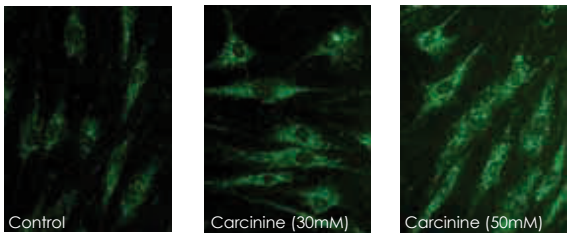
Hence, Carcinine has anti-inflammatory and soothing properties comparable to corticoids without the severe side effects.

The skin is soothed.



Carcinine energizes the skin

Sirtuins are proteins involved in aging, stress resistance and cell metabolism through their ability to maintain ATP levels.

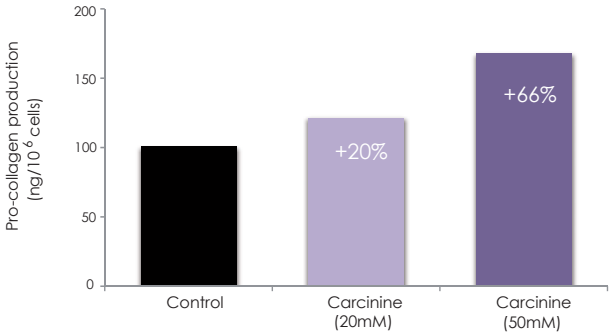


Carcinine stimulates the production of sirtuins in a dose dependant manner, hence enhancing skin cells metabolic abilities.

The skin is energized.

Carcinine stimulates collagen production

With age, the collagen production is reduced, the firmness of the skin is reduced, wrinkles appear.



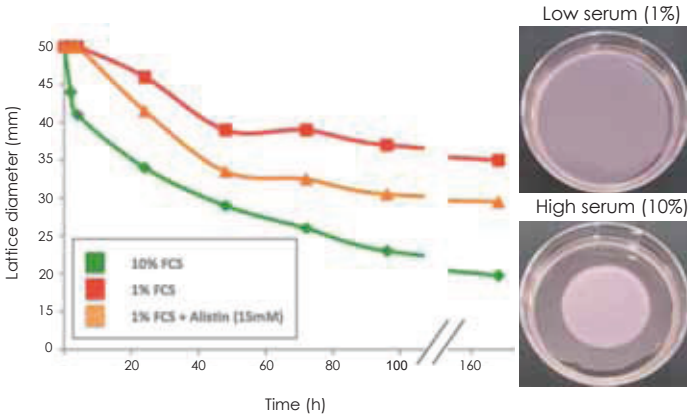
Carcinine stimulates fibroblastic collagen production in a dose dependant manner.

The skin is denser.

Carcinine increases skin firmness

With age, fibroblasts' firming abilities decrease. Using collagen lattice, an in vitro model of dermis, we measured the ability of primary fibroblasts to contract the collagen fibers. Hence, for fibroblasts in low serum media (1%), representative of an aged dermis, the lattice contraction is much slower than in a high serum media (10%) which is representative of a young dermis.
Treatment of serum deprived fibroblasts with Carcinine accelerated the lattice contraction, showing that Carcinine has firming abilities.

The skin is firmer, younger.



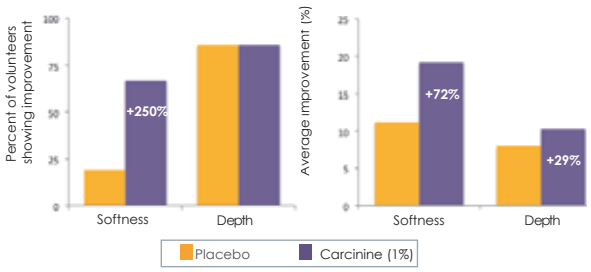
[CARCININE]

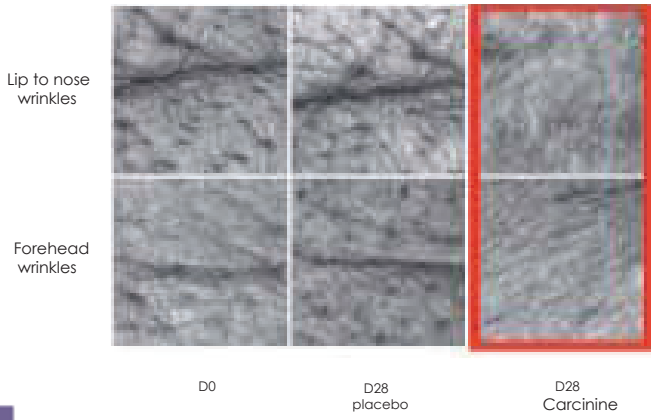
Carcinin dermalogical control on wrinkles

Carcinine reduces deep wrinkles

A 28 days treatment with Carcinine visibly reduced wrinkles. Of the 21 volunteers, 67% showed a visual improvement after the treatment with Carcinine.

The skin is smoother, softer and visibly youger.



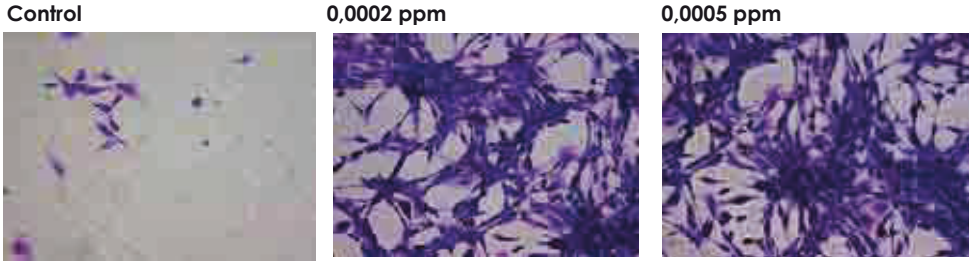


[CG-βFGF GROWTH FACTOR]

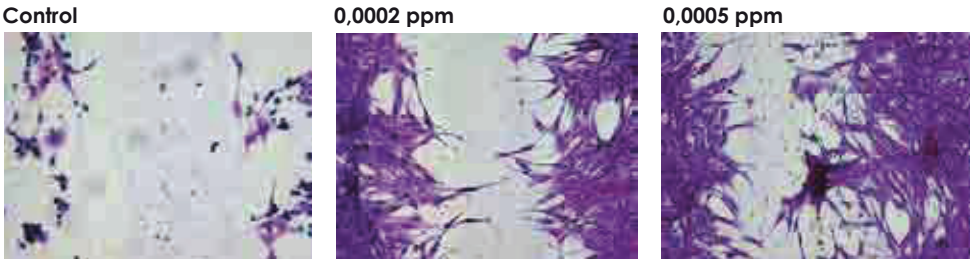
Name: Sh-polypeptide-1
Effect: Anti-ageing & anti-wrinkles
Actively generates new skin cells reducing wrinkles, accelarates wound healing and repair. Induces the synthesis of collagen and elastin.
Source: E.coli
Vectorisation: nanosome
Dosis in F-LIFT+ FACE: 0,20 %

Clinical trials
Modelates the skin rejuvenation by stimulation of cell proliferation. It increased up to **320%** the cell growth with Hace T keratinocyte cell line after 72 hours treatment at a concentration of **0,005 ppm (=5ng/ml)**.

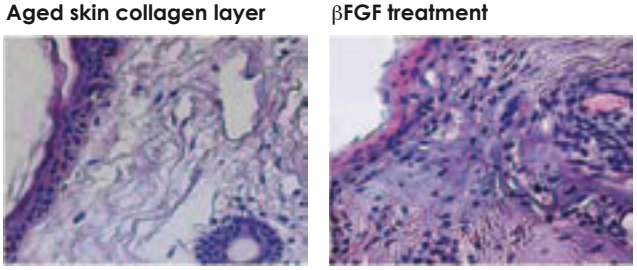
It increased up to **550%** the cell growth with fibroblast cell line after 72 hours treatment at a concentration of **0,005 ppm (=5ng/ml)**.



Morphological Change of Fibroblast cell
Cell morphology changed after 72hr incubation with CG-βFGF in the condition of serum free medium.



Cell migration was performed with fibroblast cell after treatment with CG-βFGF. After seeding fibroblast cell in a 60 mm culture plate, culturing for 24hrs, scrapping up cells by scraper and then treating βFGF. The state of cell migration was observed in a week. The enhancement of fibroblast cell migration by CG-βFGF was observed under microscope after staining with SRB. βFGF treatment greatly enhanced the migration of fibroblast cell compared to control.



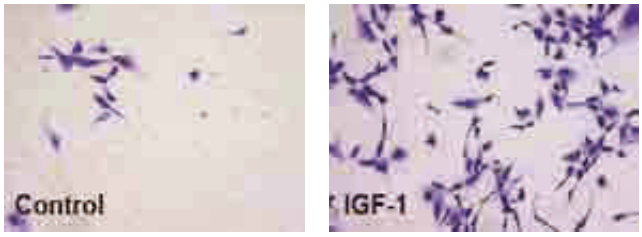
By inducing βFGF into the skin tissue, dermis section showed more collagen extensions.

[CG-IGF1 GROWTH FACTOR]

Name: Sh-oligopeptide-24
Effect: Anti-wrinkles & fat burning
Treat the appearance of lines and wrinkles. Increases skin's own collagen & elastin levels and reduce blotchiness. Refines texture glide effectively and slim the face with a fat burning effect
Source: E.coli
Vectorisation: nanosome
Dosis in F-LIFT+ FACE: 0,25 %

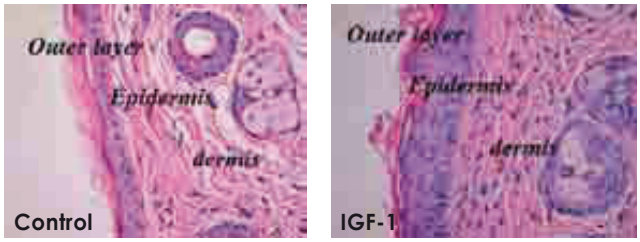
Clinical trials
Modelates the skin rejuvenation by stimulation of cell proliferation. It increased up to **290%** the cell growth with fibroblast cell line after 72 hours treatment at a concentration of **0,01 ppm (=10ng/ml)**.

Morphological Change of Fibroblast cell



Cell morphology changed after 72hr incubation with CG-IGF-1 (10ng/ml) on fibroblast cell line.

Skin Histology with CG-IGF-1



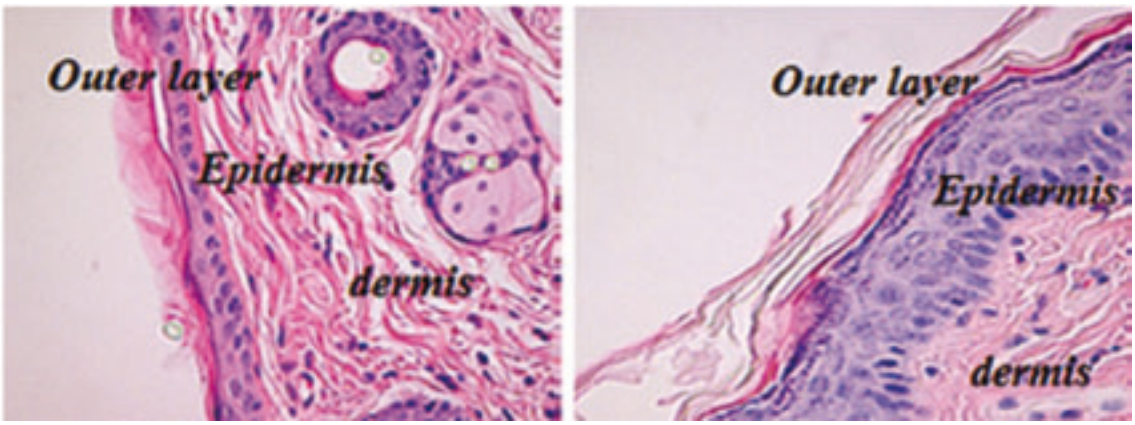
The microscopic image (X400) of skin section of histochemical staining for histology after 5 days treatment with CG-IGF-1 nanosome containing cream.

[CG-TRX GROWTH FACTOR]

Name: Sh-polypeptide-2
Effect: Anti-oxidant & anti-wrinkles
Strong anti-oxidant that reduces free radicals and inhibits the aged skin cells. Visibly provide a luminous and up lifted complexion by reinforcing skin's defenses. Reduces and prevents lines and wrinkles by actively generating new skin cells.
Source: E.coli
Vectorisation: nanosome
Dosis in F-LIFT+ FACE: 0,20 %

Clinical trials
Modelates the skin rejuvenation by stimulation of cell proliferation. It increased up to **180%** the cell growth with fibroblast cell line after CG-TRX treatment after 72 hours treatment at a concentration of **0,005 ppm (=5ng/ml)**.

Skin histology with CG-TRX



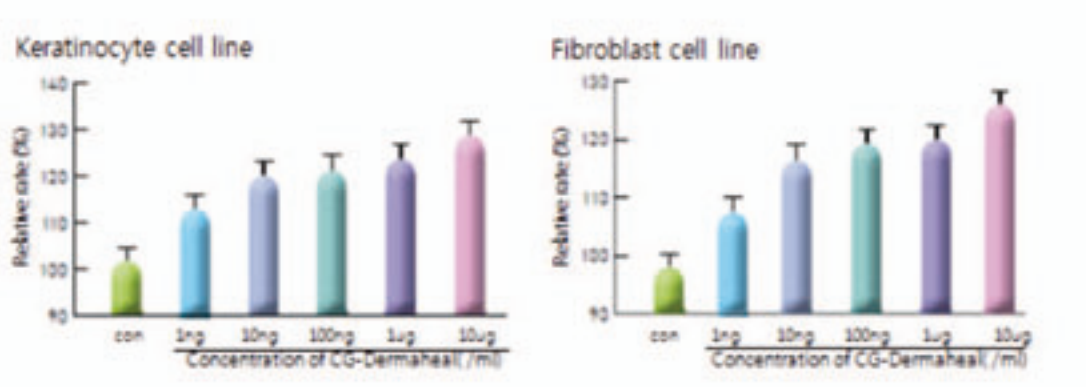
Microscopic image (x400) of skin section after 5 days treatment with CG-TRX

[CG-EDP3 GROWTH FACTOR]

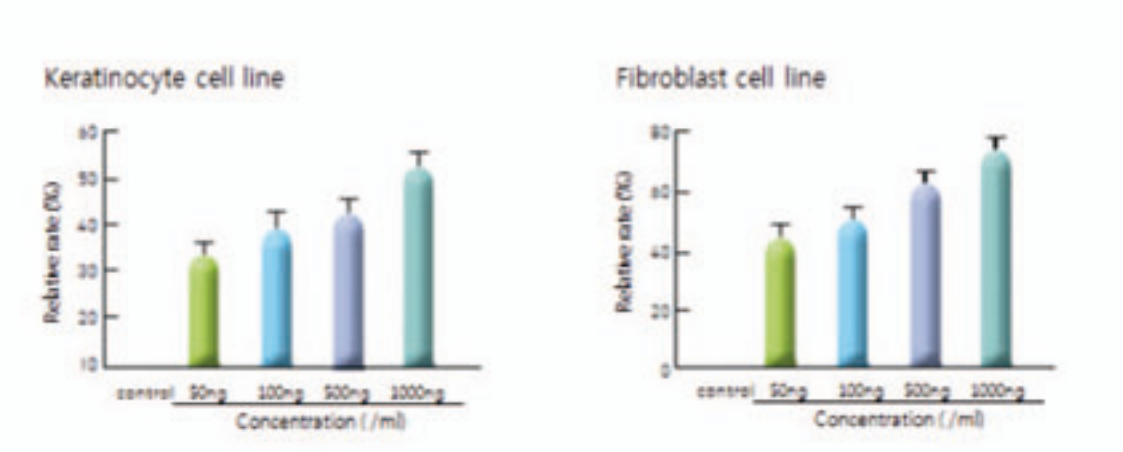
Name: Oligopeptide-24
Effect: Skin firming & anti-wrinkles
- Reduces and prevents lines and wrinkles by actively generating new skin cells.
- Enhances skin tone that brimming with vitality and energy.
- Minimize scars on skin by forming new skin cell.
- Up-regulation of cell growth and migration, cell survival, extracellular matrix expression.

Source: Chemical synthesis
Vectorisation: nanosome
Dosis in F-LIFT+ FACE: 0,25 %

Clinical trials
Signal Transduction and Signaling Pathway of CG-EDP3



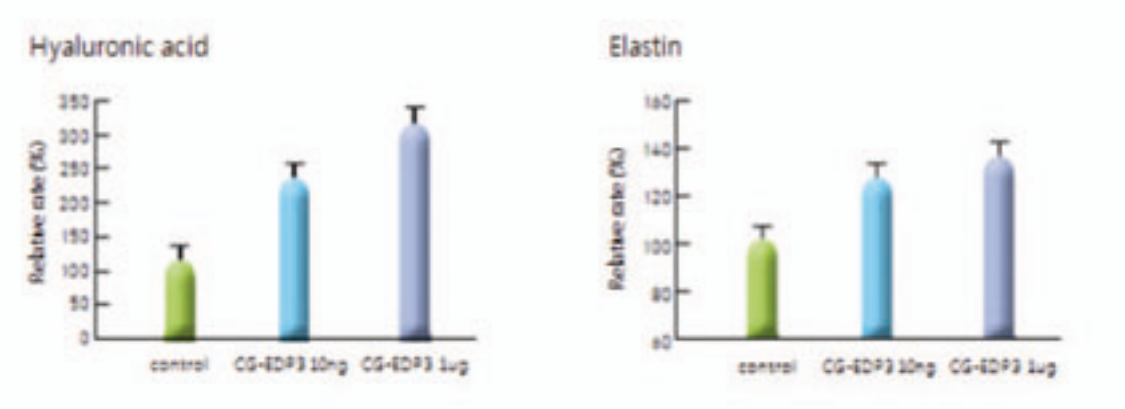
Cell Proliferation with Keratinocyte and Fibroblast Cells



The enhancement of NIH3T3 fibroblasts and HacaT keratinocytes proliferation by CG-EDP3 was quantified by SRB assay at OD590nm. CG-EDP3 increased NIH3T3 fibroblasts and HacaT kerati-nocytes proliferation in dose-dependent manner.

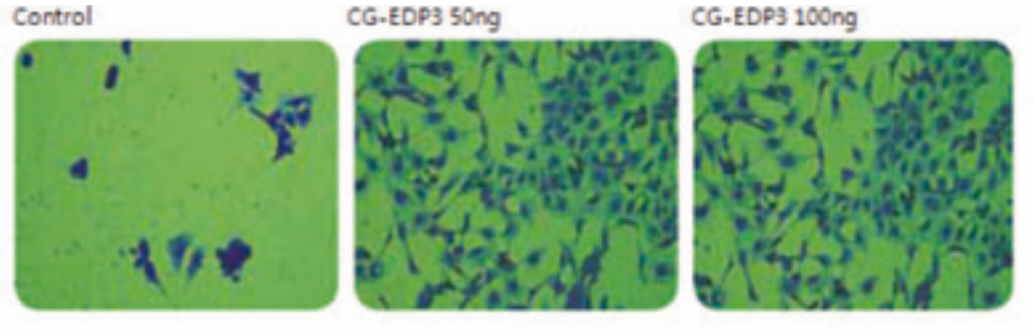
[CG-EDP3 GROWTH FACTOR]

Regulation of Hyaluronic Acid and Elastin Expression



CG-EDP3 showed positive regulation of Hyaluronic acid and Fibronectin expression. Increased expression of hyaluronic acid (3 folds) and Elastin (1.3 fold) was observed in dose-dependent manner with CG-EDP3 in fibroblast cell in ELISA assay.

Morphological Change of Fibroblast Cell



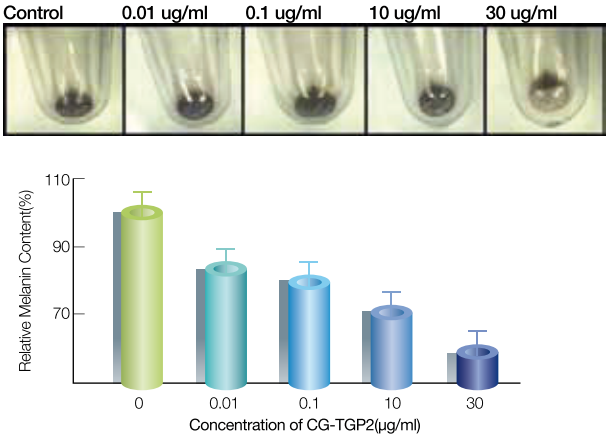
Cell morphology changed by CG-EDP3 treatment after 72hr in the condition of serum free medium.

[CG-TGP2 GROWTH FACTOR]

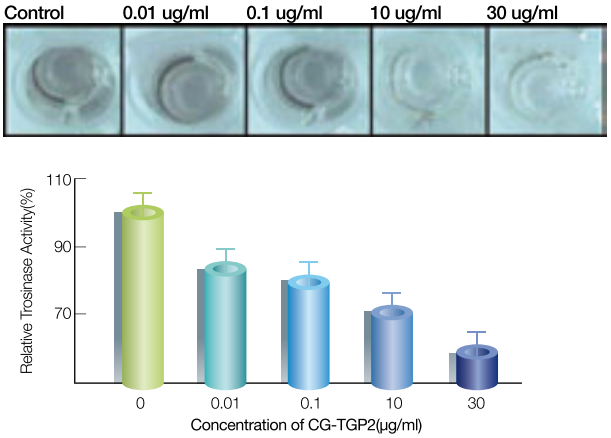
Name: Oligopeptide-34
Effect: Skin lightening, anti-atopic dermatitis, anti-wrinkles
- Decrease expression level of TRP1, tyrosinase and TRP2.
- Inhibit melanosome transfer to keratinocyte.
- Restrain the proliferation of activated T cell and inhibit expression of the TH1 type «proinflammatory cytokine».
Vectorisation: nanosome
Dosis in F-LIFT+ FACE: 0,25%

Clinical trials

Inhibition of melanin synthesis and tyrosinase activity by CG-TGP2.

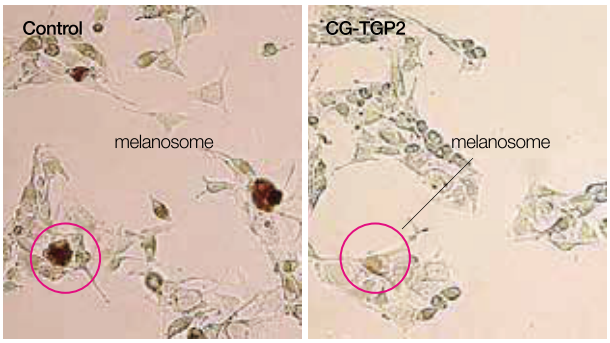


CG-TGP2 significantly inhibits melanin synthesis on melanocyte cell line in a concentration dependent manner.



The analysis of tyrosinase activity after treatment of CG-TGP2 in various concentration in melanocyte. We observe the decreased enzyme activities in a dose-dependent manner.

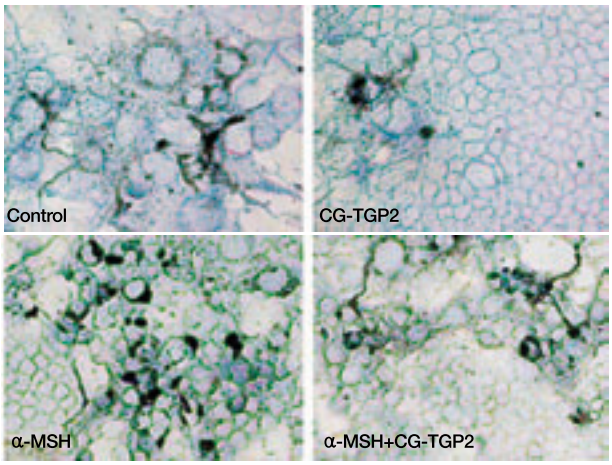
Morphological change of melanocyte cell line

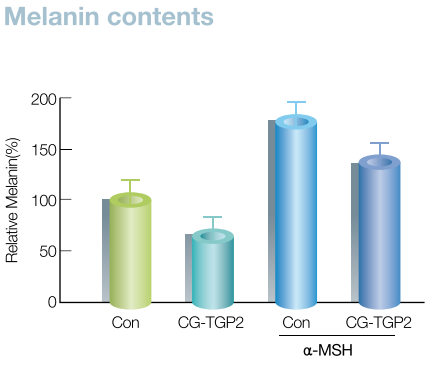


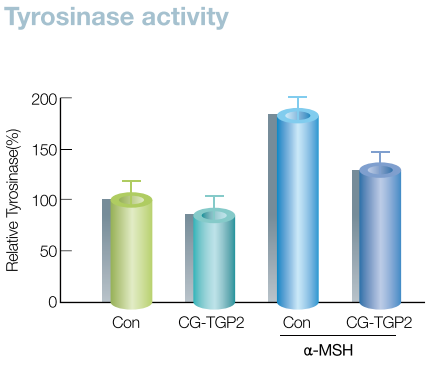
Compared to the cell morphology, we observe the decreased melanosome formation in CG-TGP2 treated melanocyte cell line.

[CG-TGP2 GROWTH FACTOR]

Inhibition of melanosome transfer in melanocyte and keratinocyte co-culture.



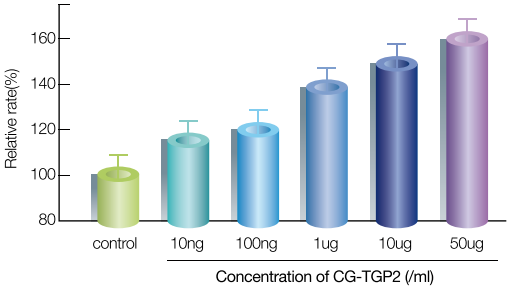




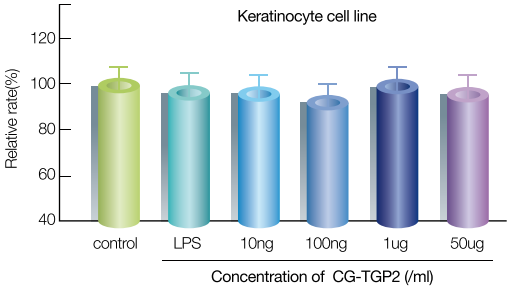
Phenotypic appearance of melanosome transfer in co-cultured cell lines with melanocyte and keratinocyte. Representative morphologies of co-cultures were observed under microscopy (x100) which was exposed for 4 days with 200 ng/ml a-MSH and 30 microg/ml CG/TGP. We observed that CG-TGP2 was blocking melanosome transfer to keratinocyte layer in normal and a-MSH treated cell lines.

Increase cell proliferation with CG-TGP2

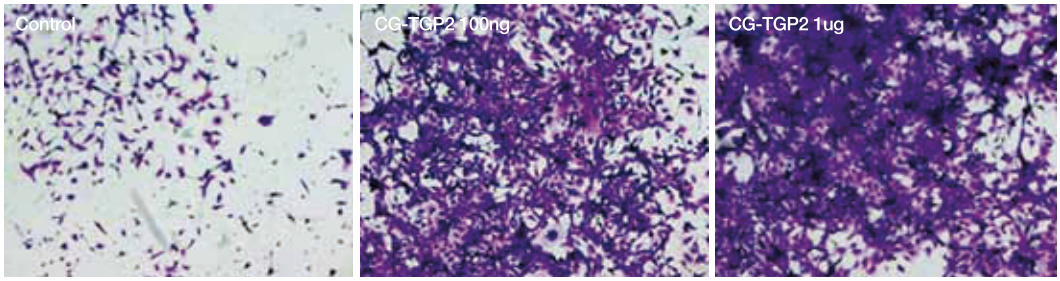
Cell growth assay with fibroblast cell line
after CG-TGP2 treatment for 72hrs.



No effect on Keratinoyte cell growth.



Morphological change of fibroblast cells with CG-TGP2

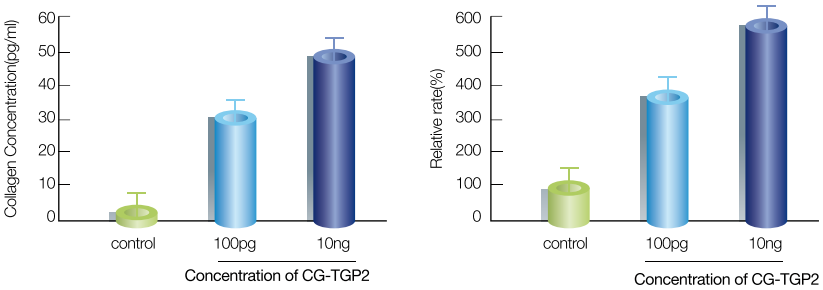


Cell morphology change after 72hrs incubation with CG-TGP2 (100ng/ml) in the condition of serum free media culture.

[CG-TGP2 GROWTH FACTOR]

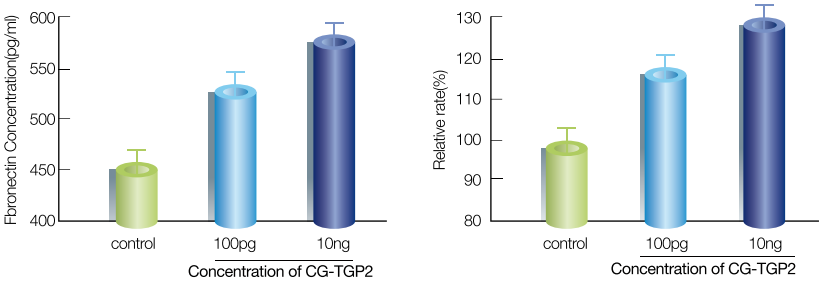
Regulation of collagen and fibronectin expression with CG-TGP2

Collagen synthesis



Shows collagen increase of 550% in expression compared to control when CG-TGP2 is added in the fibroblast cell line.

Fibronectin synthesis



Shows fibronectin increase of 128% in expression compared to control when added CG-TGP2 is added in the fibroblast cell line.