

[F-XFC FACE]

Product identity

F-XFC FACE formula is the ultimate anti-ageing treatment. Each vial is containing only the pure active ingredients, without any preservatives or other chemicals. This formula is mostly known from anti-ageing doctors as they commonly use it in mesotherapy for rejuvenation. Organic silicon is the main ingredient of this formula with various effects as cystostimulation, free radicals blocker, anti-glycation, anti-wrinkles, firming, collagen synthesis booster and anti-inflammatory. It's complemented to increase the skin tightening with DMAE and hyaluronic acid low molecular weight (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.
- Restores the skin structure.
- Moisturizes.
- Improves skin softness
- Soothes irritated and damaged skin.
- Reduces redness.
- Replaces or complements hyaluronic acid micro-injections.



Active ingredients

- DMAE 0,5%
- Organic silicon 0,5%
- Hyaluronic acid 0,10%

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 0.05 cc.
- Technique: Epidermic mesotherapy, Nappage, Papule.
- Needle: 30G.

Can be mixed with:

- 10 to 20% F-Vitamin AC E (for bio-revitalisation).
- 10 to 20% F-Vitamin C 20% (for little sun damage).

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.

[F-XFC+ FACE]

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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 to 27 G.

Can be mixed with:

10 to 20% F-Vitamin AC E (for bio-revitalisation).
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About XFC FACE system

Presentation:

The skin is the largest organ, accounting for about 16 % of your total body weight. The principal functions of the skin are to protect our body against water loss (desiccation) and against mechanical impacts and UV-light from outside. Several layers form the skin. The outermost layer of the epidermis (Stratum corneum) is the protective shield, responsible for the barrier effect against water loss from inside and UV-light from outside. The lower epidermis layer and the dermis are important for skin structure. Skin aging is a biochemical process that principally takes place in the lower epidermis and in the dermis.

Ageing is mainly due to the following phenomenons which are globally treated by the ingredients contained in the XFC FACE system: **(Figure 1: action mechanism of XFC FACE system)**

- Destruction of the extracellular matrix, increased breakdown and glycation of the proteins (collagen, elastin etc.) imparting firmness and elasticity to the skin. (1)
- Lower production of collagen by the fibroblast. (2)
- Destruction of cellular junctions. (3)
- Transepidermic water loss. (4)
- Oxidative stress produced by the accumulation of free radicals, exposure to UV-light and physical or nervous strain induce the production of interleukins producing skin inflammation, reduction of the skin defences, collagen and cellular membrane lipids degradation. (5)
- Reduction of water retention in the dermis. (6)

Focus on free radicals (Figure 2: inflammation process):

Free radicals are atoms or molecules with one or 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 3: 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 trigger 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.*

Our XFC FACE system is responding and fighting against each of these processes responsible of skin ageing. It's an ultimate treatment to prevent, to stop and to reverse skin ageing. XFC FACE system is based on 3 molecules: organic silicon, DMAE and hyaluronic acid. Each of these ingredients is playing an important role in our global anti-ageing treatment program.

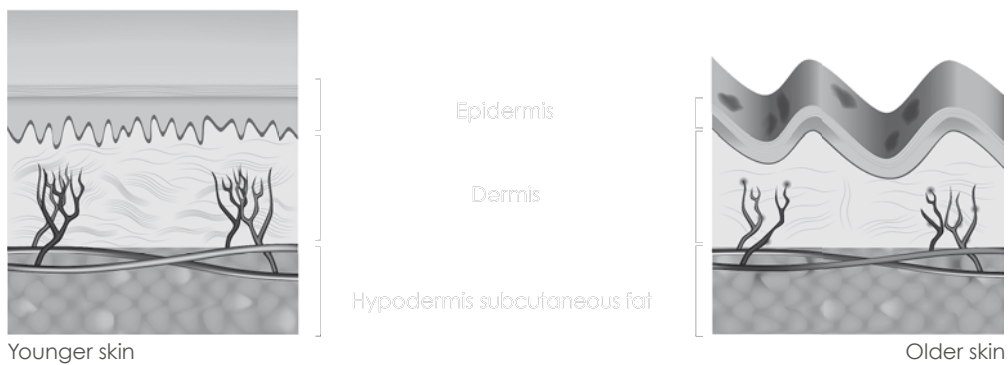
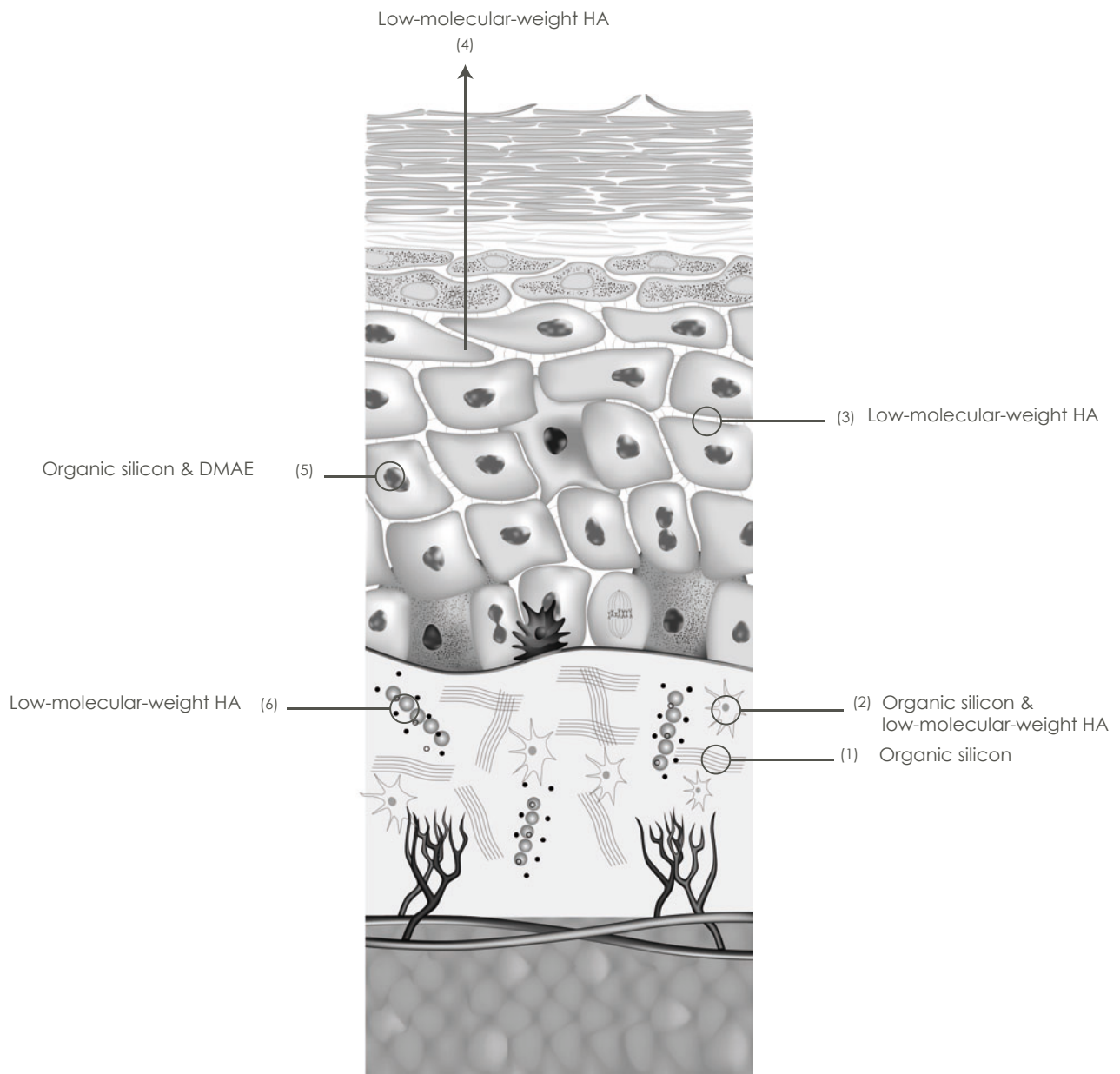


Figure 1: action mechanism of XFC FACE system.

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.

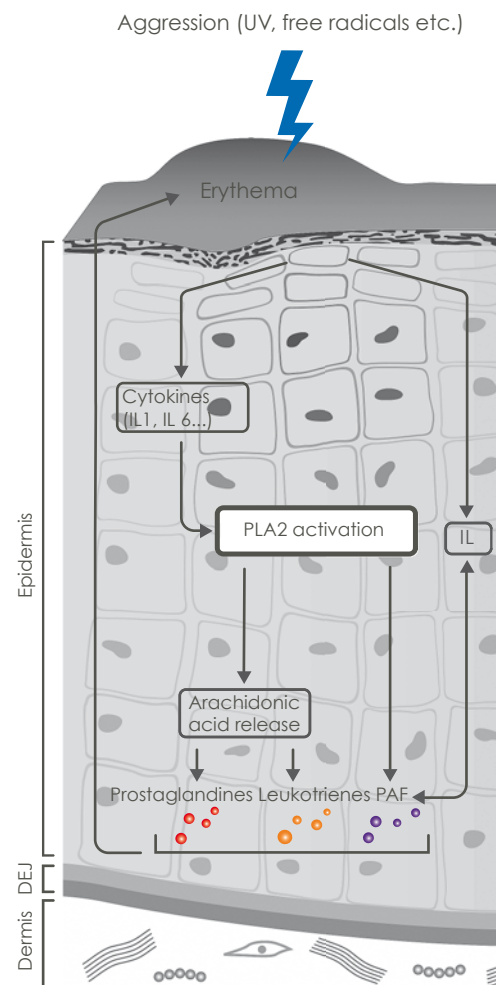
XFC FACE system focus on two inflammation mediators: cytokines and lipidic mediators. Cytokines are soluble proteins or glycoproteins, synthesised, stored and carried by immune cells (lymphocytes, monocytes and activated macrophages) as well as skin cells (keratinocytes and fibroblasts). Cytokines are 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.

XFC FACE system has been proved to reduce IL1, IL6 gene expression and 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.

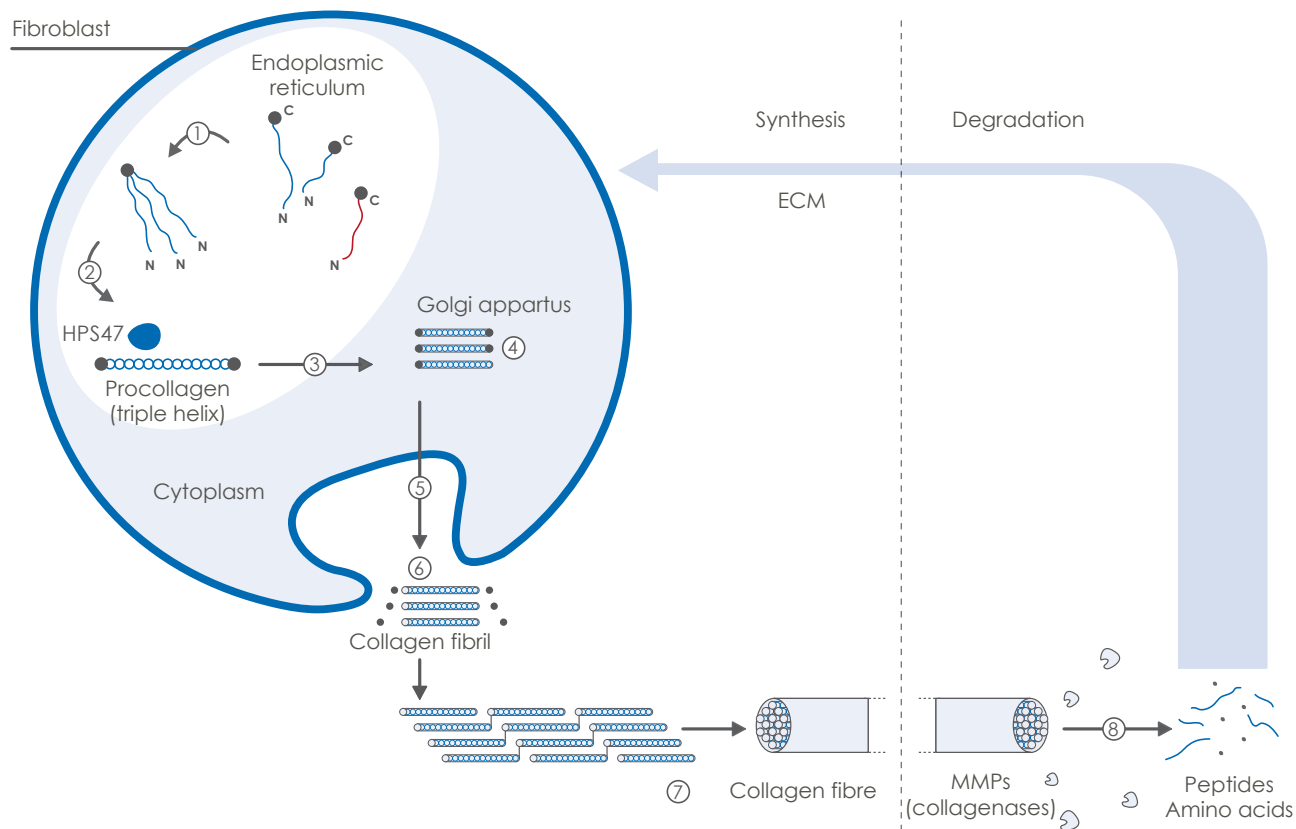
Amplification

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 2: inflammation process.



Collagen structure is made of three α polypeptidic chains of repeated units of Glycine, Proline and Hydroxyproline. Procα 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 bonds (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 3: cycle of collagen.

Organic silicon (Methylsilanol mannuronate):

Our organic silicon is a semi-natural silanol. Silanols are organic derivatives of silicon, with many hydroxyl functions and are synthesized in the presence of different radicals, which confer stability and specificity to the compound. They all possess their own unique biological properties, enhanced for some of them by the presence of these radicals. Concerning our compound, the radical is mannuronic acid, extracted from laminaria, a brown alga. Silicon is a constitutive element of the cutaneous connective tissue, which takes part in the formation and organization of the extra-cellular matrix (ECM). The natural concentration in silicon decreases with ageing and leads to tissue destruction: aged skin and wrinkles. Silanols are capable to substitute this loss in silicon and thus help in restructuring connective tissue by slowing down the effects of aging. The activity of organic silicon was proven through the restructuring of the connective tissue and the multiple related effects (anti-wrinkles, firming, stimulation, anti-glycation, oxidative stress reduction, moisturizing).

Fibroblast cyto stimulation inducing collagen synthesis to firm, smooth the skin and reduces the wrinkles.

Cutaneous cells cyto stimulation, in particular for fibroblasts, is a key factor of the young connective tissue. The silanols respond to this need by stimulating fibroblasts division, thus they contribute to maintain a normal cellular metabolism in aging tissue. Silanols effects on collagen production, skin tightening and young skin aspect, are a direct consequence of their cyto stimulating effects, demonstrated on fibroblasts cultures. The regeneration of the connective tissue helps to firm, smooth the skin and reduce the wrinkles. Silanols reduce up to 30% deep wrinkles and 25% of medium wrinkles.

Anti-glycation

The glycation is a reaction between sugars (or all other aldehydes) and a protein leading to protein alteration. This reaction, activated by free radicals and oxidative stress, is also called the Maillard reaction. All the proteins and in particular, the cutaneous proteins (collagen, elastin, enzymes...) are concerned by the glycation which results in a loss of elasticity, and the tissue rigidification but also a loss of enzymatic activity leading finally to skin ageing. Silanols are well known for their anti-glycation properties. They protect specific proteins sites and play an effect on carbohydrate oxidation products (e.g. 6PG or glucose-6-phosphate). The anti-glycation activity of our organic silicon was demonstrated on a reference protein (BSA) submitted to glycation by glucose.

Oxidative stress reduction

Due to their cell membranes affinity, the silanols, and particularly our organic silicon are capable to reorganize and to reinforce these membrane structures against free radicals attacks. Moreover, they have a free radical scavenger activity due to the presence of mannuronic acid. Our tests have shown that they present an anti-inflammatory and soothing activity characterized in vitro by a decrease in interleukins production. In vivo, it protects from cell infiltration and apparition of the characteristic inflammation signs as erythema and oedema.

Skin moisture

Due to the presence of hydroxyl groups and water molecules in their chemical structure, the silanols possess a good moisturizing activity. Concerning our organic silicon, the polyosidic structure of the mannuronic radical participates in a complementary way to keep water inside the tissues. The moisturizing effect was demonstrated by infrared, hydroxyl functions form hydrogen bonds with water and there is an additional effect of the specific radical (alginate acid). The persistent moisturizing activity one week after the end of the treatment is the direct consequence of the tissue regeneration occurring right after skin application of silanols.

DMAE (Dimethyl MEA):

Dimethylaminoethanol, better known as DMAE, is an antioxidant, cellular membrane stabilizer and muscle tightener. It helps to firm, smooth and brighten the skin. It also enhances the effects of other antioxidants.

Cellular membrane stabilizer & free radical scavenger

DMAE's antioxidant action comes from this ability to strengthen the cell membrane. DMAE can do this because its structure allows it to insert itself between components of the cell plasma membrane and help protect the cell from free radical attack. When DMAE acts as an antioxidant and keeps the cell membrane intact, it reduces oxidative stress and inhibits production of arachidonic acid and interleukins responsible of inflammation.

Muscle tightener

Muscles contract when the brain sends a signal to the targeted muscle. The signal travels along a nerve, which ends a short distance before it makes contact with the muscle. At the tip of the nerve is a bulb full of chemicals including acetylcholine. The nerve releases the chemicals, and they trigger the muscle to contract. Acetylcholine is an important component of this process because it acts as a "wake up call" for the muscles. When acetylcholine makes contact with the muscles, the muscles respond with tone and movement. However, both the production of this important chemical and its effect on the muscles decrease as the body ages. This is one reason muscles start to lose their tone. When muscles behind the face lose tone, the skin begins to sag. In addition to DMAE's antioxidant role in protecting the cell membrane from attack by free radicals, it also fights against sagging muscles. DMAE does this by promoting the production of acetylcholine. By triggering a response that tones the muscles, the result can be firmer, smoother skin with fewer wrinkles and less skin sagging.

Low-molecular-weight hyaluronic acid (Sodium hyaluronate):

Our low-molecular-weight hyaluronic acid (certified Ecocert) 15.000 - 50.000 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.

Levels of activity:

- Free radical scavenger.
- Reduction of oxidative stress.
- Reduction of inflammation process by modulation of Interleukin expression and protection the fibroblast membranes.
- Reduction of glycation.
- Skin tightening, reduction of wrinkles and fine lines.
- Stimulation of fibroblast and collagen production.
- Reorganisation of dermal matrix.
- Reinforcement of cellular junctions, reduction of the transepidermic water loss and improvement of the skin moisture.

Clinical results:

XFC FACE synergic effect against free radicals and oxidative stress to reduce inflammation process (interleukin-1 limitation, cellular membrane protection, lipids peroxidation protection, interleukin 6 limitation).

Organic silicon potential evaluation on avoiding IL-1 expression.

After incubation with different concentrations of silicium, UV exposed keratinocytes express up to 60% less IL-1 (**Figure 4: IL-1 expression limitation by organic silicon**). Cytokines, such as IL-1, activate the epidermal growth factor (EGF) receptor on the surface of the fibroblasts. The tyrosine kinase on the intracellular side phosphorylates the mitogen-activated protein (MAP) kinase, which finally activates the transcription factors, activator protein-1 (AP-1) and nuclear factor kappa B (NF-kappaB). Both factors increase the expression of matrix metalloproteinases (MMP), which degrade collagen. AP-1 additionally down-regulates the expression of collagen. This mechanism confers to organic silicon a soothing and protective action against inflammatory response, collagen degradation and down regulation.

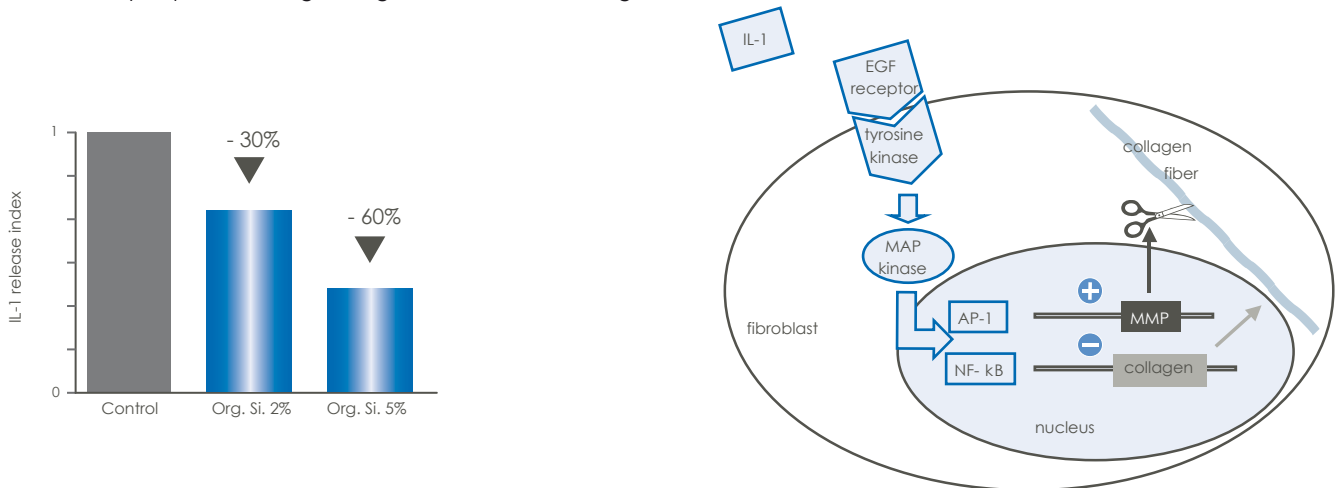


Figure 4: IL-1 expression limitation by organic silicon.

Evaluation of organic silicon potential on cellular membrane protection and reinforcement.

After incubation with different concentrations of organic silicon, an increase of cell's membrane order is observed, that optimizes cells protection against free radicals. Organic silicon increases membrane resistance (**Figure 5: membrane reinforcement and protection by organic silicon & DMAE**). In the XFC FACE system this effect is more over increased in presence of vectorized DMAE. Structure of DMAE allows it to insert itself between components of the cell plasma membrane and help protect the cell from free radical attack as the organic silicon. When organic silicon and vectorized DMAE keep the cell membrane intact, the oxidative stress is reduced and the production of arachidonic acid and interleukins responsible of inflammation are inhibited.

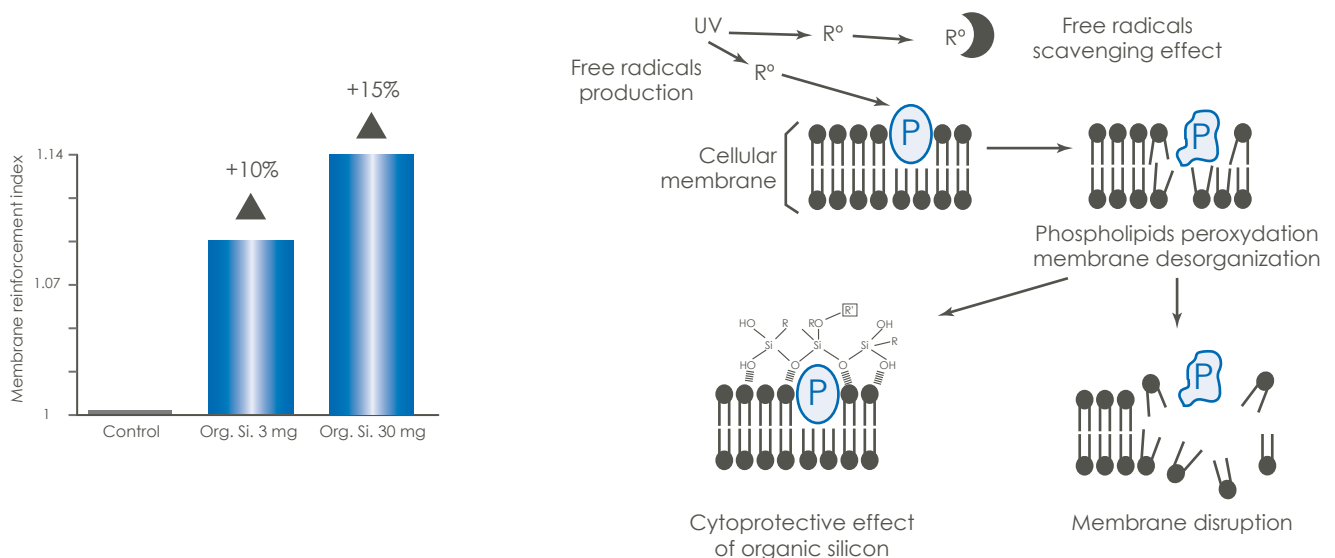


Figure 5: membrane reinforcement and protection by organic silicon & DMAE.

Anti-glycation effect of organic silicon, potential against the generation of cross-linked collagen.

The glycation is a reaction between sugars (or other aldehydes) and a protein leading to protein alteration. This reaction, activated by free radicals and oxidative stress, is also called the Maillard reaction. All the proteins and in particular, the cutaneous proteins (collagen, elastin, enzymes...) are concerned by the glycation which results in a loss of elasticity, and to the tissue rigidification but also to a loss of enzymatic activity leading finally to skin ageing. The anti-glycation activity of organic silicon was demonstrated on collagen submitted to glycation by HNE (**Figure 6: anti-glycation effect of organic silicon**). Organic silicon protects specific proteins sites and plays an effect on carbohydrate oxidation products.

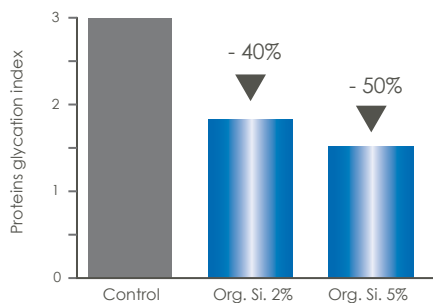


Figure 6: anti-glycation effect of organic silicon.

Anti-wrinkle effect of organic silicon.

Wrinkles formation is essentially due to a decrease in skin cells metabolism and a destruction of the supporting tissue. Estimation of "around the eyes wrinkles" (surface, medium or deep) was realized in vivo, from prints and macrophotographs. These tests have demonstrated that organic silicon have a smoothing effect at the surface level after 12 weeks treatment (**Figure 7: anti-wrinkles effect of organic silicon**), due essentially to their regenerative activity on deep wrinkles.

Macrophotographs of the crow's feet are taken with a digital camera in standardized conditions before and after 12 weeks treatment.

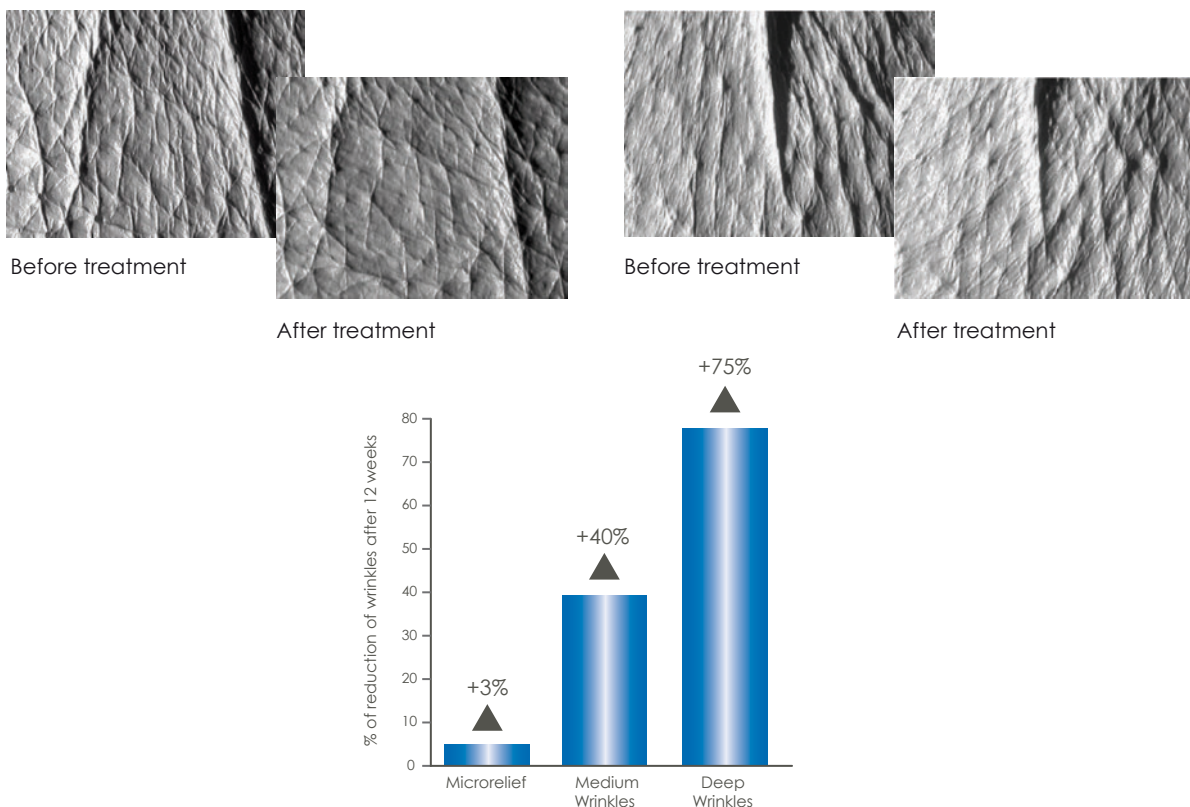


Figure 7: anti-wrinkle effect of organic silicon.

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: $\frac{[\text{produced PIP}] - [\text{control PIP}]}{[\text{control PIP}]} \times 100$. The result was an improvement of collagen I synthesis of more than 21%.

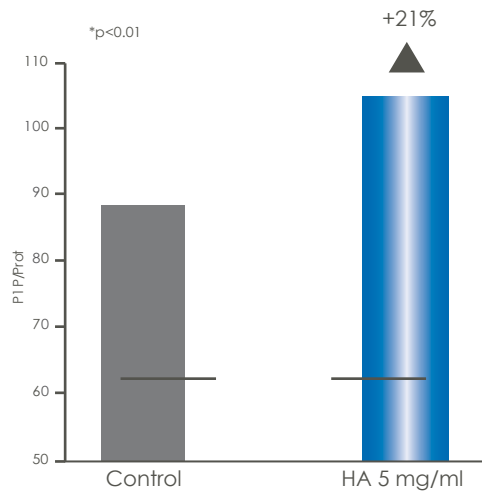


Figure 8: low-molecular-weight hyaluronic acid collagen stimulation effect.

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.

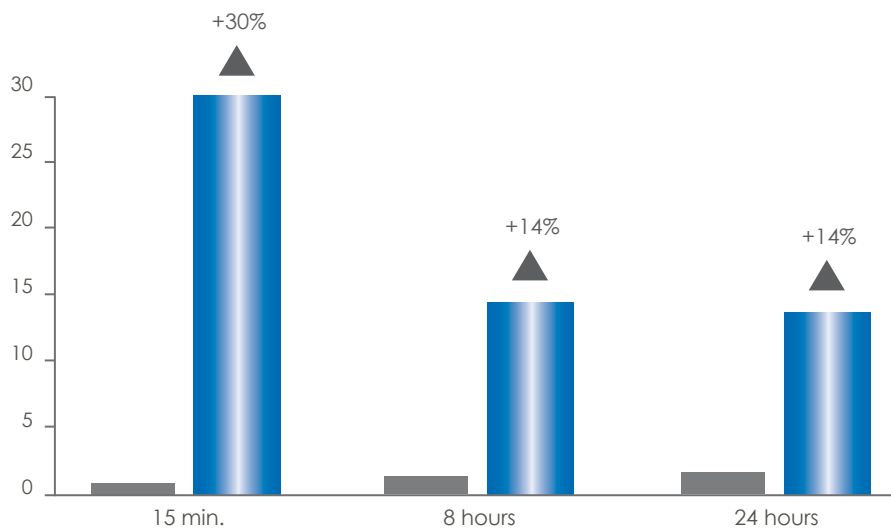


Figure 9: low-molecular-weight hyaluronic acid moisturizing test.