INSTITUT ESTHEDERM
PARIS

ECOBIOLOGICAL APPROACH TO SKIN SAGGING

RESTARTING SKIN'S NATURAL TIGHTENING MECHANISMS

Multi-level stimulation of five collagens by biomimetic peptides

The core of NAOS research
UNDERSTANDING OF SKIN AGING

Since they were founded, NAOS Laboratories (Bioderma, Institut Esthederm, Etat Pur) have distinguished ourselves through recognized expertise in the fields of biology, dermatology, aesthetics and health.
Our research is nourished by a singular, scientific approach to living things: **ECOBIOLOGY**. This approach considers the skin as an ecosystem whose natural mechanisms need to be protected, strengthened or stimulated, in order to preserve its long-term health and beauty.

As a specialist in skin aging, Institut Esthederm goes beyond simply correcting the signs of aging: by mastering the causes of skin imbalances, it's possible to develop innovative ecobiological solutions capable of strengthening the skin's defense and self-regeneration mechanisms.

NAOS Laboratories design **innovative technologies based on biomimetic active ingredients** for Institut Esthederm that target one or more biological pathways to correct skin dysfunctions and guarantee long-lasting skin youthfulness.

Élodie Valin,
NAOS Scientific Valorization Director

ECOBIOLOGY APPLIED TO SKIN SAGGING

INTENSIVE PRO-COLLAGEN+

OVERALL REVITALIZATION OF SKIN FIRMNESS: ACT ON THE "EPIDERMIS – DERMAL-EPIDERMAL JUNCTION – DERMIS" SUPPORT ECOSYSTEM

Pro-firming efficacy on the skin's tightening mechanisms

INSTITUT ESTHEDERM has identified biomimetic peptides capable of stimulating the synthesis of five major collagen types involved in skin firmness in order to optimize the volume of the various skin layers and the interactions between them.

Restarting the structural network, as well as exchanges and cohesion between the different tissue layers, lastingly tightens skin architecture and helps optimize skin firmness.

C O N T E N T S

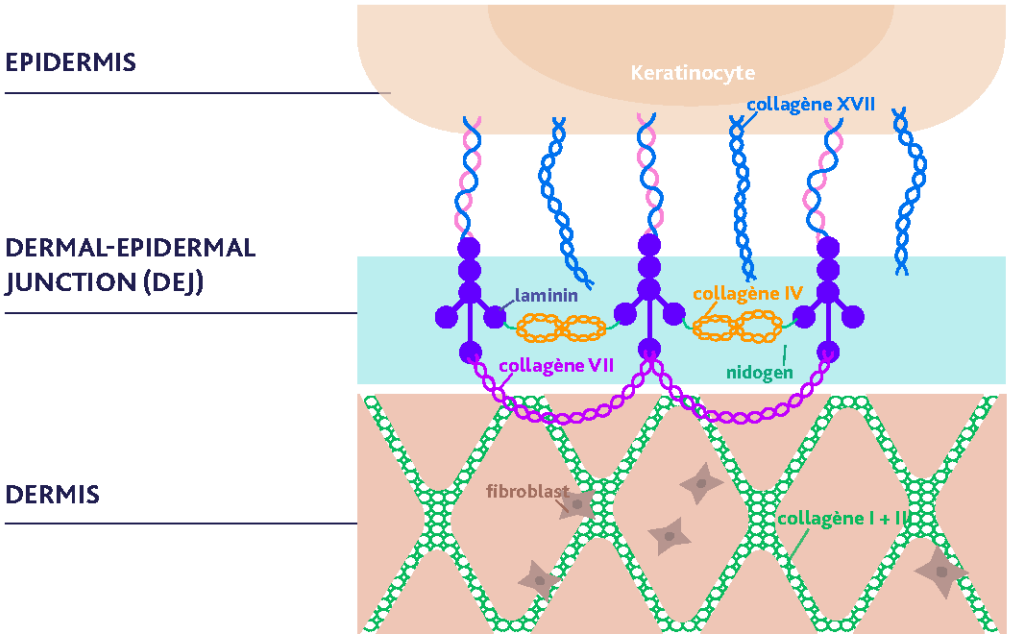
1 - FIRMNESS:

A PROCESS INVOLVING ALL SKIN LAYERS

The skin's firmness and density depend on the quantity and quality of the proteins that contribute to its volume, strength and resistance[1], as well as on the dynamics of interactions between the epidermis – dermal-epidermal junction (DEJ) – dermis structures. For a smoothing effect on the surface of the epidermis, the dermis must be organized into networks of fibers and interact with the different layers of the skin, particularly thanks to a cohesive and functional DEJ.

At the heart of this virtuous dynamic is an interdependent network of vital proteins: collagens. While collagens I and III create dermal density, the collagen XVII located in the epidermis and collagens IV and VII in the dermal-epidermal junction play a central role in dynamic interactions between the different skin layers.

Targeting dermal collagens in isolation is not enough to guarantee overall, long-lasting efficacy: the skin collagen ecosystem must be involved. These complementary actions require a comprehensive corrective response to the dysfunctions involved in the skin ecosystem's sagging.



2 - THE ECOBIOLOGICAL APPROACH: RESTARTING THE COLLAGEN ECOSYSTEM INVOLVED IN THE SKIN'S SUPPORT MECHANISMS

For many years, cosmetic science has been interested in stimulating type I or III dermal collagen to restore skin firmness. Institut Esthederm's ecobiological approach restores overall tightness to the ecosystem responsible for skin firmness, by stimulating types IV and VII collagen in the dermal-epidermal junction (DEJ) and type XVII epidermal collagen, involved in tissue interactions and skin resistance mechanisms.

With age, the loss of adhesion surface between different skin structures is a major cause of skin aging. Alteration of the various types of collagen contributes to the disorganization of all the skin's foundations: interactions decrease, nutritional exchanges are impoverished, sagging sets in, and wrinkles deepen.
Restoring the anchorage between each skin layer by stimulating different types of collagen and adhesion proteins (integrins, laminin and fibronectin) helps restore overall tightness, for firmer skin:

- increases dermal volume for a visible smoothing action on the surface,
- restructures epidermal and dermal anchoring structures to optimize exchanges and the quality of the skin's support mechanisms.

LOSS OF COLLAGEN FUNCTION

Age-related intrinsic biological changes

In the course of chronological aging, collagen production declines and its degradation increases, leading to a reduction in the overall quantity and quality of collagens.
The concentration of collagens in adolescent skin is 80% type I and 15% type III, then changes in adulthood (type I: 85%; type III: 8-11%).

At the end of growth, fibroblasts become less active and collagen production declines by 1 to 1.5% per year.
Histologically, young skin has intact, abundant, tight and well-organized collagen fibrils, whereas collagen fibrils in older skin are fragmented and coarsely distributed[2].

• A less dynamic epidermis

Collagen XVII decline contributes to the fragility of the structures that support keratinocytes at the DEJ. The epidermis is less able to renew itself.

• A looser dermal-epidermal junction

With aging, its disorganization contributes to skin sagging[3]: the DEJ flattens considerably with age, and the exchanges are altered.

Recent studies show that the organization of the dermal-epidermal junction is closely linked to the different types of collagen that make up the dermis and the DEJ.

Reduced levels of collagens IV and VII lead to anchoring fibril destabilization, contributing to the breakdown of the skin network with aging[4].

• Disorganized, atrophied dermis

The decrease in extracellular components, particularly type I collagen, leads to progressive dermal atrophy and disorganization[5]. Skin volume decreases[6]. Anisotropy, or the directional organization of fibers, is impacted.

Decreased biosynthesis of type I and III collagens is linked to a reduction in the number of dermal fibroblasts and their loss of efficacy[7].
At the same time, several parameters accelerate collagen degradation:

- inhibition of TGF-ß growth factors, a major regulator of dermal matrix biosynthesis, which controls collagen homeostasis[2],
- increase in collagenases, matrix metalloproteinase (MMP) enzymes, which accelerate the progressive fragmentation of collagens in the dermis[8].

The influence of hormonal impregnation

Estrogen levels influence dynamic collagen synthesis in the skin.

- **Puberty**

The changes brought about by the production of sex hormones in teenagers lead to rapid and extensive renewal of collagen, particularly type I collagen, which is essential for growth.

- **Pregnancy**

Collagen and elastin undergo a marked increase followed by a rapid decrease during the post-partum period. As with teenagers, increased levels of circulating cortisol can weaken collagen fiber synthesis, making them less resistant to stretching and causing stretch marks.

- **Menopause**

Estrogen depletion and deprivation lead to a reduction in the skin's collagen content: - 2.1% in collagen and - 1.13% in skin thickness per year for 15–18 years after menopause[9]. Several studies support the anti-aging properties of estrogen treatments in postmenopausal women, showing a positive effect on collagen quantity, skin thickness, elasticity and hydration, as well as improved wound healing[10].

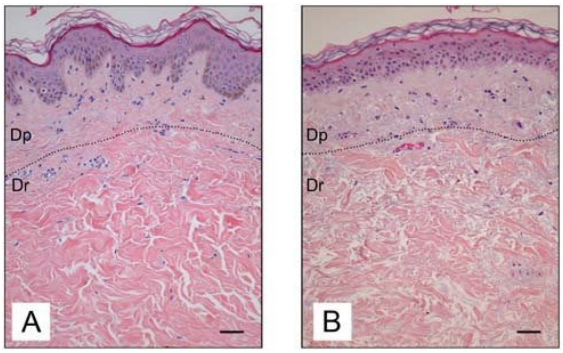
Extrinsic changes: The environment

The exposome, an aggravating factor in sagging, UV rays, pollution and smoking all have a harmful effect on skin collagen. Their cumulative effects over decades are responsible for accelerated sagging.
The main culprits are Reactive Oxygen Species (ROS), which threaten the integrity and levels of collagen in the extracellular matrix.

The metabolism of skin collagens is affected by protein carbonylation, leading to irreversible loss of functionality.

YOUNG SKIN
The optimal exchange surface between epidermis and dermis is provided by the DEJ, which allows the passage of elements essential to epidermal quality.

OLD SKIN
The DEJ flattens out, interactions no longer occur or are decreased, the ecosystem becomes disorganized and ptosis sets in.



Intrinsic and extrinsic alterations in skin collagen synthesis lead to disorganization and loss of functionality.

Their structure is more fragile and brittle, resulting in visible clinical signs:

- **increased skin rigidity**
- **changes to skin thickness**
- **reduced biomechanical properties**
- **loss of skin firmness and tone**
- **appearance of facial ptosis**

3 - COLLAGENS:
AN INTERDEPENDENT ECOSYSTEM

COLLAGEN, A MAJOR SKIN-FIRMING PROTEIN

Skin collagens, in particular type I and III dermal collagens, compose up to 90% of the dermis, providing firmness and resistance. The synthesis, quality and organizational structure of collagen naturally deteriorate with age, leading to skin sagging.

STRENGTH, STRUCTURAL COHESION: EPIDERMAL AND DEJ COLLAGENS

Type IV and VII collagens are part of the DEJ and play an important role in epidermal-dermal cohesion. Collagen XVII contributes to the overall structure of the epidermis and its anchoring to the DEJ.

- **Collagen XVII**

This transmembrane collagen helps anchor the epidermis at the dermal-epidermal junction. It contributes to the skin's structural integrity by maintaining tissue cohesion. It also plays a key role in epidermal homeostasis, including stem cell renewal and keratinocyte proliferation and differentiation[11].
Collagen XVII is also involved in epidermal stability and signal transmission between cells and the extracellular matrix[12].

Stimulating the production of collagen XVII strengthens the cohesion between epidermis and dermis, increases skin resistance and contributes to epidermal homeostasis for smoother-looking skin.

- **Collagens IV and VII**

They are essential components of the dermal-epidermal junction (DEJ). They support the basal layer of the epidermis, anchor dermal collagens and play a crucial role in skin integrity. The structure of collagen IV is more flexible and folded than that of the other collagens[13].
Collagen VII also plays a role in dermal extracellular matrix stability: it links type I and type III collagens[14].

The DEJ plays a major role in the exchange of nutrients, oxygen, water, ions and "signal" molecules such as cytokines, hormones, growth factors and more between the epidermis and dermis. Certain adhesion proteins, such as integrins, laminins, nidogen and fibronectin, contribute to this DEJ functionality.

Stimulating the production of collagens IV and VII, as well as certain adhesion proteins (integrins, laminins, nidogen, fibronectin) contributes to skin structure stability and improves skin's resistance to age-related physiological distension.
Since the DEJ is involved in cell regulation, these collagens provide a favorable environment for cell exchanges between the epidermis and dermis.

FIRMNESS: DERMAL COLLAGENS

In adult skin, the most abundant collagens are type I (80%), type III (10%), and type V (<5%)[15].

- **Collagen I** forms fibrils that combine into thick, highly resistant fiber bundles[16] essential for maintaining dermal density and preventing skin sagging.
- **Collagen III** is characterized by finer, more flexible fibrils. It combines with collagen I to form a dense structure that contributes to dermal volume, particularly involved in fiber diameter determination, conferring suppleness and a plump appearance to the skin[17]. It is associated with the skin's remodeling and repair phases. In particular, it is synthesized in greater quantities to support healing and make way for collagen I in the remodeling phase.

The 3D structure of dermal collagens and their adhesion to the extracellular matrix and the DEJ are also provided by key proteins such as **fibronectin and integrins**.

Stimulating the production of collagens I and III, as well as their adhesion proteins (fibronectin, integrins), improves skin firmness and helps increase dermal density, resulting in tighter, smoother-looking skin.

To correct the clinical signs of sagging skin *(loss of firmness, elasticity, facial ptosis)*.
Biomimetic active ingredients stimulate production of five collagens involved at every level of skin architecture, optimizing the structure and functionality of the skin's firmness ecosystem.

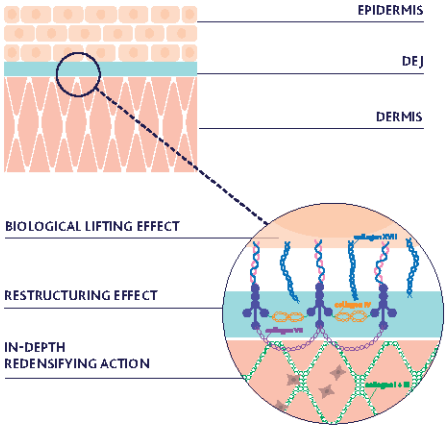
4 - PROCOLL+ TECHNOLOGY

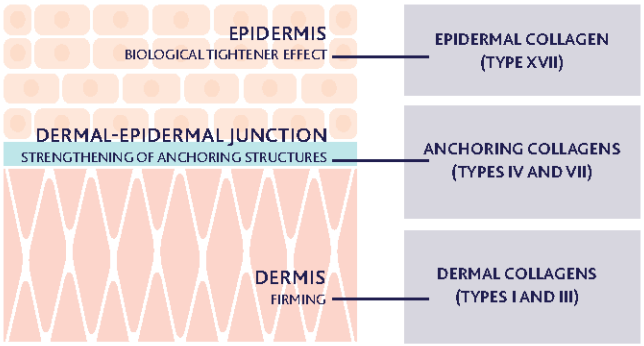
Multi-level action on support structure components for lasting, overall results on skin firmness.

Stimulation of 5 collagens as well as structural proteins in the different skin layers guarantees efficacy across the skin's entire support architecture.
Restoring dermal volume combined with stimulating the epidermis-dermis anchoring structures (DEJ) reinforces the skin's natural tightening and firming mechanisms.

AN INNOVATIVE MODE OF ACTION

Multi-level efficacy restarts the major biological mechanisms involved in the skin's ecosystem of tightness, density and resistance.





ACTION ON THE EPIDERMIS + THE DERMAL-EPIDERMAL JUNCTION

- **Stimulation of collagen XVII and DEJ structural proteins** such as laminin and nidogen: helps strengthen epidermal-DEJ anchoring, epidermal resistance and cell renewal quality, for a "biological tightener" result.
- **Stimulation and protection of collagens IV and VI:** optimizes the epidermis-dermis exchange surface, for a more dynamic skin architecture.

ACTION ON THE DERMIS

- **Stimulation of collagen types I and III:** firming action and increased dermal volume.
- **Stimulation of structural glycoproteins (ß-1 integrin, fibronectin):** protects 3D dermal collagen architecture for functional tissue reorganization.

BIOMIMETIC ACTIVE INGREDIENTS FOR VISIBLE EFFICACY ON SKIN SAGGING

BIOMIMETIC PEPTIDES, selected for their complementary action—both quantitative and qualitative—on the skin's various support structures:

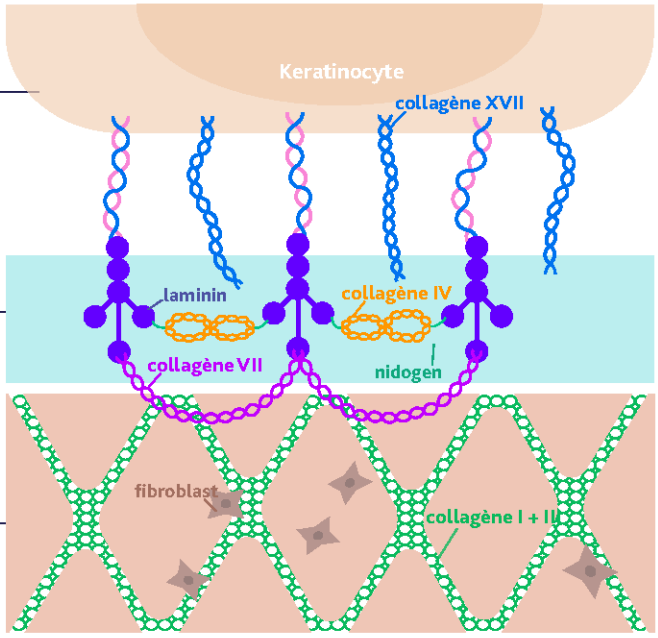
- biological stimulation of multiple collagens I, III, IV, VII, XVII
- stimulation of glycoproteins involved in 3D collagen tissue architecture

XYLOSE, A VEGETABLE SUGAR, preserves the quality of epidermis-dermis anchoring structures and their function as biological tighteners, guaranteeing skin cohesion and resistance.

EPIDERMIS

DERMAL-EPIDERMAL JUNCTION (DEJ)

DERMIS



Stimulation of epidermal collagen XVII

Protection of epidermal collagen XVII

Stimulation of DEJ collagens IV, VII

Stimulation of DEJ structural glycoproteins:
Laminin-5, nidogen, ß-1 integrin

Stimulation of dermal collagens I, III

Stimulation of structural glycoproteins in the extracellular matrix:
Fibronectin, ß-1 integrin

INTENSIVE
PRO-COLLAGEN+
SERUM

RESTARTING THE FACIAL CONTOUR'S BIOLOGICAL TIGHTENING MECHANISMS

INDICATIONS

Skin sagging.
All skin types.

PHARMACEUTICAL FORM

Fast absorbing, fresh, transparent aqueous gel.
Immediate tightening effect.

INSTRUCTIONS FOR USE

Apply morning and evening to face and neck.
Alone or in addition to INTENSIVE PRO-COLLAGEN+ cream.

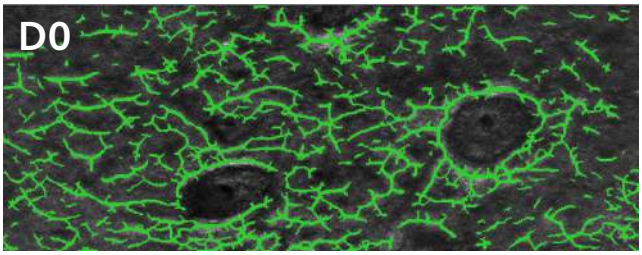
PRESENTATION

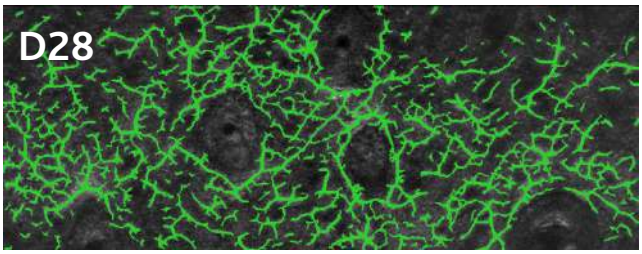
30 ml pump bottle

XYLOSE	Biomimetic sugar protects collagen XVII (epidermal)	1.5%
PALMITOYL TRIPEPTIDE-1 + PALMITOYL TETRAPEPTIDE-7	Biomimetic peptides boost collagens XVII (epidermal), IV and VII (DEJ), and I (dermal)	4.5 PPM
HEXAPEPTIDE-9	Biomimetic peptide boosts collagens I and III (dermal), and IV (DEJ)	0.75 PPM
ACETYL TETRAPEPTIDE-9	Collagen I booster peptide (dermal)	3.3 PPM

CLINICAL EFFICACY: MICRO-RELIEF RESTRUCTURING IMPROVES SKIN FIRMNESS

+14%[1] DIRECTIONAL REORGANIZATION OF FIBERS AFTER 1 MONTH





A more organized dermal network promotes optimal structure and tightening.

Improvement in dermal fiber network organization observed with confocal microscopy on the cheekbone after just 28 days of twice-daily application of INTENSIVE PRO-COLLAGEN+ Serum.

CLINICAL EFFICACY AT D56

+26% FIRMNESS [2]
+20% TIGHTENING EFFECT [3]
-9% FACIAL CONTOUR PTOSIS [3]

Use test under dermatological supervision. [1] Instrumental evaluation, 29 subjects, aged 46-70, twice-daily application for 28 days. [2] Instrumental evaluation, 31 subjects, aged 45-70, twice-daily application for 56 days. [3] Clinical scoring, 31 subjects, aged 45-70, twice-daily application for 56 days.

VOLUNTEER SELF-ASSESSMENT

Immediate effect after product application[4]:

88% SKIN SMOOTHED

After 2 months of use[5]:

100% MORE TONED SKIN
100% SMOOTHER SKIN
94% REDUCED WRINKLES
87% SKIN LOOKS LIFTED
84% FACIAL CONTOUR DEFINED

Use test under dermatological supervision, % satisfaction. [4] 32 subjects, 1 application. [5] 31 subjects,56 days.

SKIN TOLERANCE

Very good tolerance at D28

INTENSIVE
PRO-COLLAGEN+
CREAM

LASTINGLY REACTIVATE THE SKIN'S NATURAL FIRMING MECHANISMS

INDICATIONS
Skin sagging.
Normal, dry and very dry skin.

PHARMACEUTICAL FORM
Non-greasy rich cream.
Long-lasting comfort.

INSTRUCTIONS FOR USE
Apply morning and evening to face and neck.
Alone or in addition to INTENSIVE PRO-COLLAGEN+ serum.

PRESENTATION
50 ml jar

XYLOSE	Biomimetic sugar protects collagen XVII (epidermal)	1%
PALMITOYL TRIPEPTIDE-1 + PALMITOYL TETRAPEPTIDE-7	Biomimetic peptides boost collagens XVII (epidermal), IV and VII (DEJ), and I (dermal)	4.5 PPM
HEXAPEPTIDE-9	Biomimetic peptide boosts collagens I and III (dermal), and IV (DEJ)	0.5 PPM
ACETYL TETRAPEPTIDE-9	Collagen I booster peptide (dermal)	3.3 PPM

CLINICAL EFFICACY
REMODELING EFFECT ON THE FACIAL CONTOUR
AFTER 2 MONTHS

Visia® photos (best case) highlighting the remodeling effect on the facial contour after 56 days of twice-daily application of INTENSIVE PRO-COLLAGEN+ cream, on 31 women, aged 45–70, with normal to very dry skin.

CLINICAL EFFICACY AT D56

+43% FIRMING EFFECT[1]
+52% TIGHTENING EFFECT[1]
+40% ELASTICITY[2]

Use test under dermatological supervision, 31 subjects, aged 47–70, twice-daily application for 56 days.
[1] Clinical scoring. [2] Instrumental evaluation.

VOLUNTEER SELF-ASSESSMENT

Immediate effect after product application[3]:

97% SMOOTHER SKIN
97% LIFTED SKIN

After 1 month of use[4]:

97% SKIN IS FIRMER

After 2 months of use[5]:

81% CONTOURS REDRAWN
90% SMOOTHER SKIN
91% YOUNGER-LOOKING SKIN

Use test under dermatological supervision, % satisfaction. [3] 32 subjects, 1 application. [4] 31 subjects, 28 days. [5] 31 subjects, 56 days.

SKIN TOLERANCE

Very good tolerance at D28

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For any requests for visuals or products or to make an appointment to try our skincare products:

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