# Clinical Evidence

Five Squirrels

## THE SYNERGY BETWEEN EXOSOMES AND POLYNUCLEOTIDES

They treat two of side of the same problem:

| Ageing Mechanism | Exosomes Target | Polynucleotides Target | Combined Effect |
|---|---|---|---|
| Cellular senescence | Reprogram cell behaviour | Reduce inflammaion + give repair substrates | **Deep senescence reversal + accelerated recovery** |
| Oxidative stress | Antioxidants delivered into cell | Reduced ROS production | **Stronger protection against DNA damage** |
| ECM decline | Boost procollagen/ elastin | Boost DEJ proteins | **More structured, thicker, firmer dermis** |
| Wound healing | Cell migration + angiogenesis | DNA for cell proliferation | **Faster and better-quality regeneration** |
| Inflammation | SASP reduction | A2A receptor anti-inflammatory pathway | **Dual-pathway anti-inflammation** |
| Skin texture | Regeneration | Corneocyte renewal | **Faster smoothing, pore reduction** |

**Exosomes = tell the fibroblast WHAT to do**
→ “Repair more, produce more collagen, stop acting old.”
**Polynucleotides = give the fibroblast WHAT it needs to do it**
→ “Here are the nucleotides, the building blocks, and the anti-inflammatory signal to help you work.”

Exosomes activate the repair programs.
Polynucleotides supply the materials to execute them.
This is a classic biological synergy: **signal + substrate → amplified regeneration.**

You get a boosted outcome because:

- Exosomes activate fibroblasts
- PDRN feeds fibroblasts
- Both reduce inflammation through different biochemical mechanisms
- Both support regenerative signalling
- Both enhance ECM architecture
- Both improve wound healing

This results in:
More collagen, more elastin, stronger DEJ, reduced senescence, smoother texture, better hydration, and faster visible improvement.
**Exosomes reprogram the skin to act younger, while polynucleotides give the skin the building blocks to rebuild itself. Together, they deliver a powerful synergy for regeneration, youthfulness, and longevity.**

# Clinical Evidence

PRODUCT, DESCRIPTION AND EVIDENCE
REFERENCE: FS10-41
PUBLISH DATE: 22/12/2025

# SUPER XO+
# LONGEVITY COMPLEX
# ULTIMATE EXOSOME & PDRN RECOVERY SYSTEM

A high-performance longevity complex designed to extend the results of cosmetic treatments and biologically age-proof your skin. This innovative serum uses vegan Polynucleotides and Exosomes, targeting the dermis to restore volume, reduce the appearance of pigmentation and pores and smooth expression lines.

## KEY BENEFITS

- Reduces wrinkle depth by up to 20% in 28 days.
- Increases skin elasticity by up to 14.1% and firmness by up to 46% after 56 days.
- Accelerates the skin's healing process by up to 72% compared to baseline conditions.
- Boosts the synthesis of new collagen type XVII by 155.8%
- Reduces the appearance of visible pores by 8.1%
- Increases moisture content by 37.2%.
- Reduced melanin formation by 43.5%

## DIRECTIONS FOR USE

Apply a pea-sized amount of serum to the treatment area. Gently massage into the skin until fully absorbed. Use morning and evening, or post-treatment to boost and prolong desired effects.

## WARNINGS

For external use only. Avoid contact with eyes. If this occurs, wash affected area thoroughly with water. If irritation occurs, discontinue use. Store this product below 40°C.

## INGREDIENTS

Aqua, Glycerin, C15-19 Alkane, Sodium Acrylates Copolymer, Hydrogenated Ethylhexyl Olivate, Centella Asiatica Leaf Extract, Coco-Caprylate/Caprate, Hydrogenated Olive Oil Unsaponifiables, Lecithin, Hydrolyzed DNA, Acetyl Hexapeptide-8, Xanthan Gum, Sclerotium Gum, Pullulan, Silica, Sodium Gluconate, Citric Acid, 1,2-Hexanediol, Sodium Phytate, Benzyl Alcohol, Dehydroacetic Acid, and Sodium Benzoate.

## ACTIVE INGREDIENTS

Glycerin 4%
Centella Asiatica Leaf Extract 1%
Pullulan 0.1%
Hydrolyzed DNA 0.03mg/L*
Acetyl Hexapeptide-8 0.0275mg/L*

## GLYCERIN

Ingredient Claims:

| | |
|---|---|
| Excellent moisturising properties | Enhances skin elasticity |
| Calms and soothes irritated skin | Promotes skin barrier function |
| Reduces trans epidermal water loss | Soothes hot or sunburned skin |

Glycerin is a humectant which is present in all-natural lipids. Derived from natural substances by hydrolysis of fats and by fermentation of sugars. This palm-free vegetable Glycerin is widely used in cosmetic products and provides the following benefits:

- Moisturising: Glycerin has excellent moisturising properties. It attracts and retains moisture from the environment, helping to hydrate the skin and prevent dryness. It forms a protective layer on the skin, reducing water loss and maintaining its natural moisture balance.

- Skin barrier repair: Glycerin can support the skin's barrier function by strengthening the outermost layer of the skin, known as the stratum corneum. This can help improve the skin's ability to retain moisture and protect it from external irritants.

- Soothing and calming: Glycerin has soothing properties that can help alleviate skin irritation, itching, and inflammation. It can be beneficial for conditions such as eczema, psoriasis, or dry, sensitive skin.

- Anti-ageing effects: Glycerin has the ability to improve the appearance of fine lines and wrinkles. By maintaining skin hydration, it can enhance the skin's elasticity and firmness, giving it a smoother and more youthful appearance.

- Compatibility with various skin types: Glycerin is generally well-tolerated by different skin types, including sensitive and acne-prone skin. It is non-comedogenic, meaning it won't clog pores or contribute to breakouts.

- Enhances product effectiveness: Glycerin is often used as a key ingredient in skincare formulations because it helps other ingredients penetrate the skin more effectively. It can enhance the delivery of active ingredients, allowing them to work more efficiently.

- Cooling effect: Glycerin has a cooling effect on the skin, making it useful in products such as facial mists or soothing gels. It can provide relief for hot or sunburned skin.

Links:
International Journal of Cosmetic Science, August 2016, ePublication
British Journal of Dermatology, July 2008, pages 23-34
Journal of Cosmetic Dermatology, June 2007, pages 75-82
Proceeding of the National Academy of Sciences, June 2003, pages 7,360-7,365
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8395744/

## CENTELLA ASIATICA LEAF EXTRACT - PLANT DERIVED EXOSOMES

Ingredient Claims:

| | |
|---|---|
| Accelerates the healing process up to +72% | Boosts DNA-repair enzyme activity by up to 83% |
| Reduces cellular markers of skin aging by up to 41% | Reduces wrinkle depth and length by up to 42.9% |
| Improves skin firmness by up to 46% in 56 days | Boosts elasticity by up to 21% for more resilient skin |

Centella Asiatica Leaf Extract, in the form of exosomes, has been clinically shown to deliver multiple skin benefits. Evidence indicates that it accelerates wound healing by up to 72%, boosts DNA-repair enzyme activity by 83%, reduces cellular markers of aging by 41%, and diminishes wrinkle depth and length by up to 42.9%. Additionally, it improves skin firmness by 46% within 56 days and enhances elasticity by 21%, contributing to a more resilient and youthful appearance.

Centella Asiatica Leaf Extract, plant-derived exosomes act as natural nanocarriers, delivering bioactive compounds directly into skin cells. They help modulate cell-to-cell communication, support collagen and elastin production, reduce inflammation, and promote skin regeneration, making them valuable in anti-ageing and reparative skincare formulations.

**What is the Cellular Senescence?**

Cellular senescence is when a cell permanently stops dividing because it is damaged, stressed, or old.

Senescent cells or “Zombie” cells are those that have stopped dividing and refuse to die. They accumulate in the body with age. Senescent cells:

- Stop functioning optimally
- Release inflammatory and tissue-damaging factors (SASP)
- Contribute to wrinkles, tissue degeneration, and age-related decline

Senescence = cellular dysfunction and deterioration.

Traditionally, this “senescent state” was thought to be permanent. However, newer research in anti-aging science shows that in some situations, senescent cells can partly recover, meaning they start functioning more normally again or stop releasing harmful signals.

**What is Fibroblast Senescence?**

Fibroblasts are the main skin cells that make collagen, elastin, and other support structures that keep skin firm, smooth, and elastic.

As we age, or when skin is repeatedly stressed by UV light, pollution, glycation, oxidative stress, or injury, fibroblasts can become senescent. This means they stop dividing and stop working properly.

Senescent fibroblasts show:

- DNA damage and shorter telomeres
- Mitochondria that no longer produce energy efficiently
- Specific “age markers” inside the cell (like p16, p21)
- A harmful secretory profile called SASP, which includes:
  - Inflammatory molecules (IL-6, IL-8, TNF-α)
  - Enzymes that break down collagen (MMP-1, MMP-3)
  - Signals that can push nearby healthy cells to also become senescent

Even though senescent fibroblasts don’t divide, they stay active and this activity is damaging. They release factors that increase inflammation, break down collagen, and slow the skin’s ability to repair itself.

**Why Reducing or Reversing Fibroblast Senescence is Beneficial?**

When senescent fibroblasts build up in the skin, they contribute directly to:

- Loss of collagen and elastin → wrinkles, sagging, and skin thinning
- Slower wound healing
- Chronic low-grade inflammation
- A weaker skin barrier
- In extreme cases, a more disease-prone environment

Research shows that reducing senescence markers, helping fibroblasts become more youthful, or removing senescent cells altogether can:
Improve collagen structure and increase dermal thickness
Enhance skin elasticity and firmness
Support faster, healthier skin repair

**What does Longevity mean?**

Longevity refers to how long a cell, tissue, or organism can remain healthy, functional, and regenerative.

In skin, longevity means:
Fibroblasts stay active and produce collagen
Low inflammation
Good repair capacity
Stable, well-organized dermal structure

Longevity = maintained function and youthfulness over time.

Reducing senescent cells or preventing their formation helps tissues stay healthier for longer—this is why anti-aging research often focuses on senolytics (removing senescent cells) and senomorphics (suppressing their harmful behaviour).

In other words, “regeneration and longevity” in the skin essentially mean maintaining fibroblasts in a youthful, functionally active, non-senescent state, so the dermis can continuously renew ECM and repair micro-damage.

**Summary:**

Senescence = cells aging badly
Longevity = cells staying youthful and functional longer

When senescence increases → Longevity decreases
When senescence decreases → Longevity increases

**What are Exosomes?**

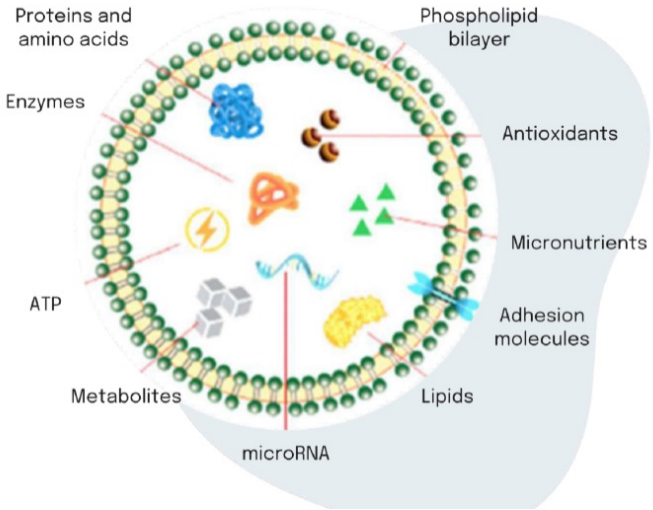
Exosomes are also known as Ectosomes or Small Extracellular Vesicles (sEVs), are tiny lipid-bilayer vesicles released by cells.

Lipid membrane-bounded extracellular vesicles of approximately 30-500 nm in diameter.
Naturally produced and secreted by all living cells (animals, plants, microorganisms).
Vital importance in cell-to-cell communication.

They carry signals (or biological messages), antioxidants, RNA, peptides, and lipids that tell skin cells how to behave.

When applied to the skin, these exosomes can enter fibroblasts and help them:
Repair damage
Reduce inflammation
Produce more collagen and elastin
Act younger and function better

In anti-ageing science, exosomes help “reprogram” or “reset” senescent skin cells.




Physico-Chemical properties

- Contain DNA, RNA, lipids, proteins, cytokines, transcription factor receptors, heat shock proteins, enzymes, antioxidants and other bioactive compounds & metabolites.
- Highly fusogenic phospho-lipid membrane

Physiological Features

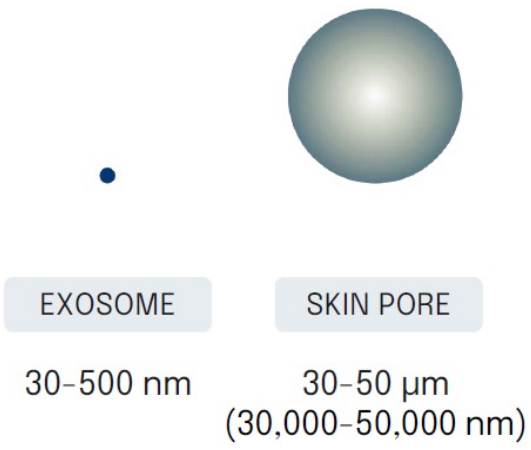
- Natural bioactive transporters
- High bio-mimicry
- Resistant to changing environmental conditions (pH, conductivity, pressure, etc)
- Permeant to cell membranes

Properties of Exosomes in skin care:

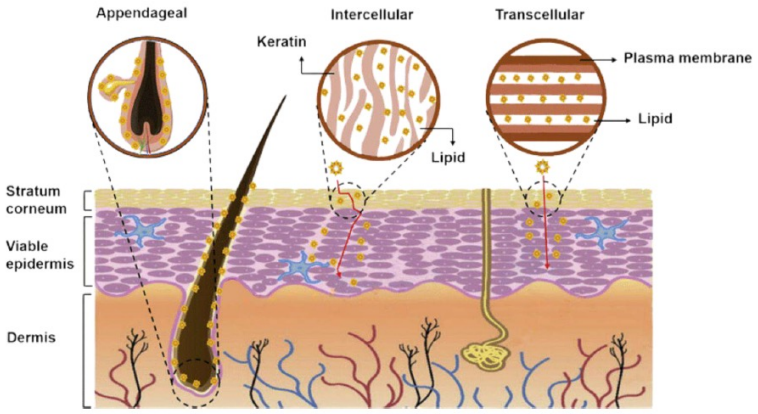
- Anti-inflammatory effect
- Redox Balance
- Immunomodulatory properties
- Healing & Hydration
- Synthesis of extracellular matrix proteins (Collagen, elastin, etc)
- Skin Protection
- Anti-ageing
- Antoxidant
- Microbiota modulation
- Regeneration
- Skin homeostasis

**How do Exosomes work?**

Exosome particles, which are smaller than skin pores, quickly penetrate the skin and provide rapid improvement effects to skin parameters.



Transdermal delivery of exosomes:




Exosomes could penetrate the stratum corneum through three pathways:

- Appendageal
- Intercellular
- Transcellular

They have a highly fusogenic phospho-lipid membranes

1. They calm inflammation
Senescent fibroblasts release many inflammatory molecules (SASP).
Centella exosomes reduce these signals and promote a more healing-focused environment.

2. They boost repair mechanisms

They increase:
- DNA repair enzymes
- Mitochondrial function
- Cellular energy

This helps stressed or aged cells regain normal activity.

3. They stimulate fibroblasts to behave like young cells
Centella exosomes increase:
- Procollagen I (up to +134%)
- Elastin (up to +126%)

This indicates fibroblasts are producing youthful ECM again.
Under the microscope, aged fibroblasts treated with Centella exosomes regain a younger-looking shape, showing partial reversal of senescence.

4. They help rebuild collagen and the extracellular matrix

They improve:
Collagen synthesis
Collagen fibre organisation
Dermal density and firmness

5. They reduce oxidative stress
Exosomes deliver antioxidants directly into cells, lowering ROS—one of the main drivers of senescence.

6. They accelerate wound healing

Centella exosomes:
Boost cell migration
Increase fibroblast and keratinocyte activity
Enhance microvascular repair

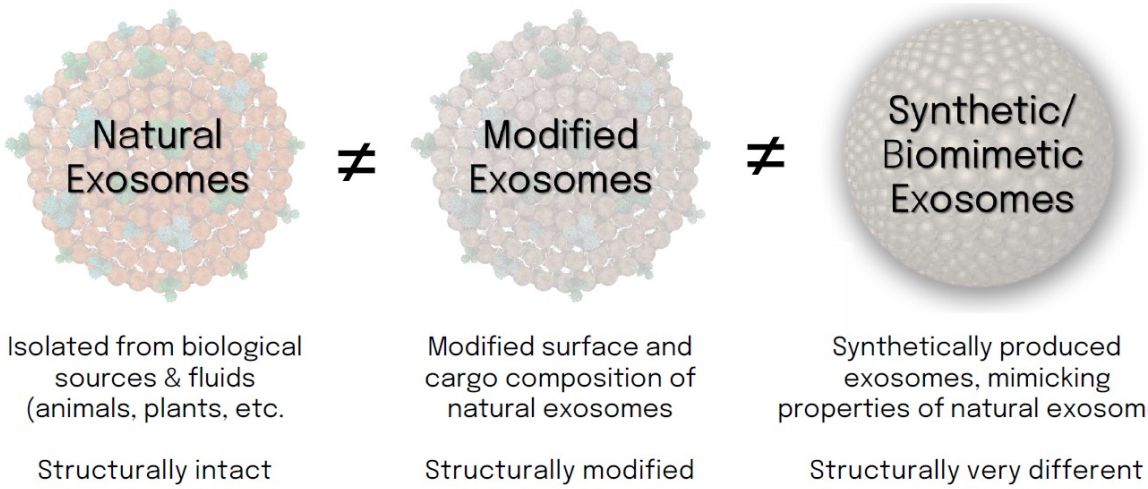
This means faster tissue renewal and better regeneration.

So, Exosomes bring healing messages to damaged fibroblasts, they reduce inflammation and oxidative stress, they activate DNA repair and cellular energy, they switch fibroblasts from “old mode” to “youthful productive mode”, they restore collagen, elastin, and tissue structure, which leads to the reversion the senescence cells and the increase of the cell longevity.

**Why choosing a plant derived exosome?**

They are from a natural source, so they are structurally intact

Comparison of the different types of Exosomes in cosmetics:




- They are structurally like mammalian exosomes, so they can penetrate and deliver molecular information to our human cells very effectively – they allow the Cross-kingdom Communication!
- They are very stable: their lipid membrane protects them from external agents and therefore protects the bioactive compounds inside
- They have a low immunogenicity, they are non-toxic and vegan friendly

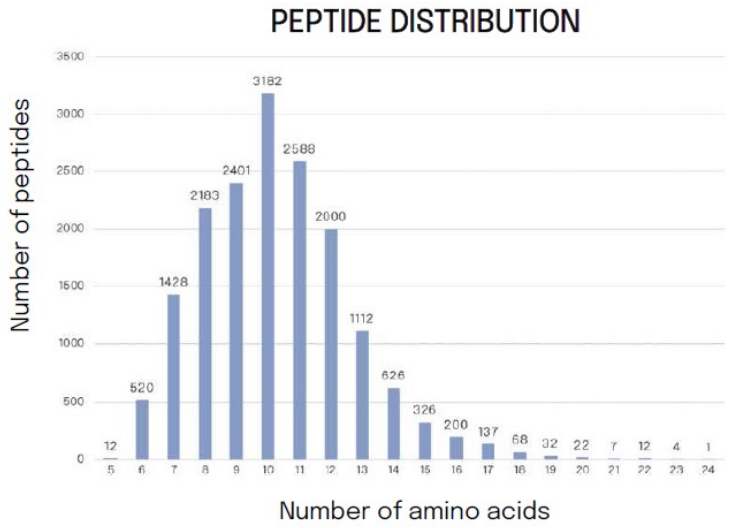
| | Plant exosomes | Mammalian exosomes | Synthetic exosomes |
|---|---|---|---|
| Secondary metabolites | 😀 | 😖 | 😖 |
| Industrial scalability | 😀 | 😖 | 😀 |
| Biomimicry | 😀 | 😀 | 😖 |
| Toxicity | 😀 | 😐 | 😖 |
| Efficacy | 😀 | 😀 | 😐 |
| Stability | 😀 | 😐 | 😀 |

Natural exosomes are not Nanoparticles, as their size is above 100nm and they are not bio persistent making them a safe material.

**Clinical Evidence/characterisation:**

>1,000 types of proteins were produced and 126 different proteins were identified in the supernatant of stem cells of Centella asiatica thanks to the proteomic analysis.

75% of naturally biosynthesized peptides are between 8-12 Aas.




**Naturally optimised peptide biosynthesis**

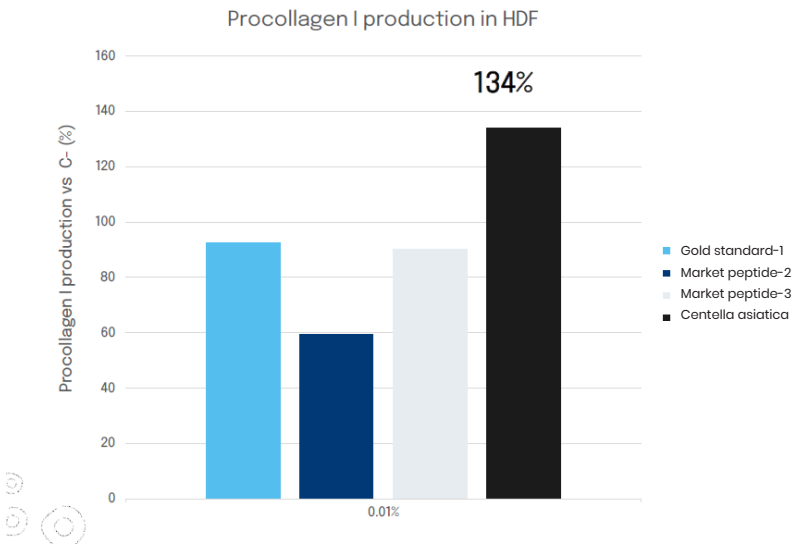
**Protein characterisation: assignment of functionality**

| GROUP | PROTEIN | ACTIVITY | REFERENCE |
|---|---|---|---|
| Metabolite interconversion enzymes | Fosfatases, Kinases | Cell to cell communication | Nguyen, L. K., Matallanas, D., Croucher, D. R., Von Kriegsheim, A., & Kholodenko, B. N. (2013). Signalling by protein phosphatases and drug development: a systems-centred view. The FEBS journal, 280(2), 751-765. |
| Protein-modifying enzymes | Proteases | Apoptosis, Plant defense system, wound healing | Salvesen, G. S., Hempel, A., & Coll, N. S. (2016). Protease signaling in animal and plant-regulated cell death. The FEBS journal, 283(14), 2577-2598. Balakireva, A. V., & Zamyatnin Jr, A. A. (2018). Indispensable role of proteases in plant innate immunity. International journal of molecular sciences, 19(2), 629. Toriseva, M., & Kähäri, V. M. (2009). Proteinases in cutaneous wound healing. Cellular and Molecular Life Sciences, 66, 203-224. |
| Cytoskeleton proteins | Actin and microtubules | Wound healing, Tissue regeneration | Abreu-Blanco, M. T., Watts, J. J., Verboon, J. M., & Parkhurst, S. M. (2012). Cytoskeleton responses in wound repair. Cellular and Molecular Life Sciences, 69, 2469-2483. Kopecki, Z., & Cowin, A. J. (2016). The role of actin remodelling proteins in wound healing and tissue regeneration. Wound Healing-New Insights into Ancient Challenge. IntechOpen, 133-154.<br>Kopecki, Z., & Cowin, A. J. (2016). The role of actin remodelling proteins in wound healing and tissue regeneration. Wound Healing-New Insights into Ancient Challenge. IntechOpen, 133-154. |
| Activity-modulating proteins | G proteins | Wound healing, cell proliferation, tissue regeneration, plant defense system, cell differentiation, cell to cell communication. | Doma, E., Rupp, C., & Baccarini, M. (2013). EGFR-ras-raf signaling in epidermal stem cells: roles in hair follicle development, regeneration, tissue remodeling and epidermal cancers. International journal of molecular sciences, 14(10), 19361-19384. Doma, E., Rupp, C., & Baccarini, M. (2013). EGFR-ras-raf signaling in epidermal stem cells: roles in hair follicle development, regeneration, tissue remodeling and epidermal cancers. International journal of molecular sciences, 14(10), 19361-19384. Doma, E., Rupp, C., & Baccarini, M. (2013). EGFR-ras-raf signaling in epidermal stem cells: roles in hair follicle development, regeneration, tissue remodeling and epidermal cancers. International journal of molecular sciences, 14(10), 19361-19384.<br>Drosten, M., Lechuga, C. G., & Barbacid, M. (2014). Ras signaling is essential for skin development. Oncogene, 33(22), 2857-2865. Cao, H., Glazebrook, J., Clarke, J. D., Volko, S., & Dong, X. (1997). The Arabidopsis NPR1 gene that controls systemic acquired resistance encodes a novel protein containing ankyrin repeats. Cell, 88(1), 57-63. Drosten, M., Lechuga, C. G., & Barbacid, M. (2014). Ras signaling is essential for skin development. Oncogene, 33(22), 2857-2865. |
| Chaperones | Chaperones | Wound healing | Scieglinska, D., Krawczyk, Z., Sojka, D. R., & Gogler-Piglowska, A. (2019). Heat shock proteins in the physiology and pathophysiology of epidermal keratinocytes. Cell Stress and Chaperones, 24(6), 1027-1044. |

Exosomes from Centella asiatica cell cultures
A concentration of: 7.5 x 1010 exosomes/ml (75.000.000.000 exosomes/ml)*
= 75 billions of exosomes/ml.
Average diameter of 148 nm.

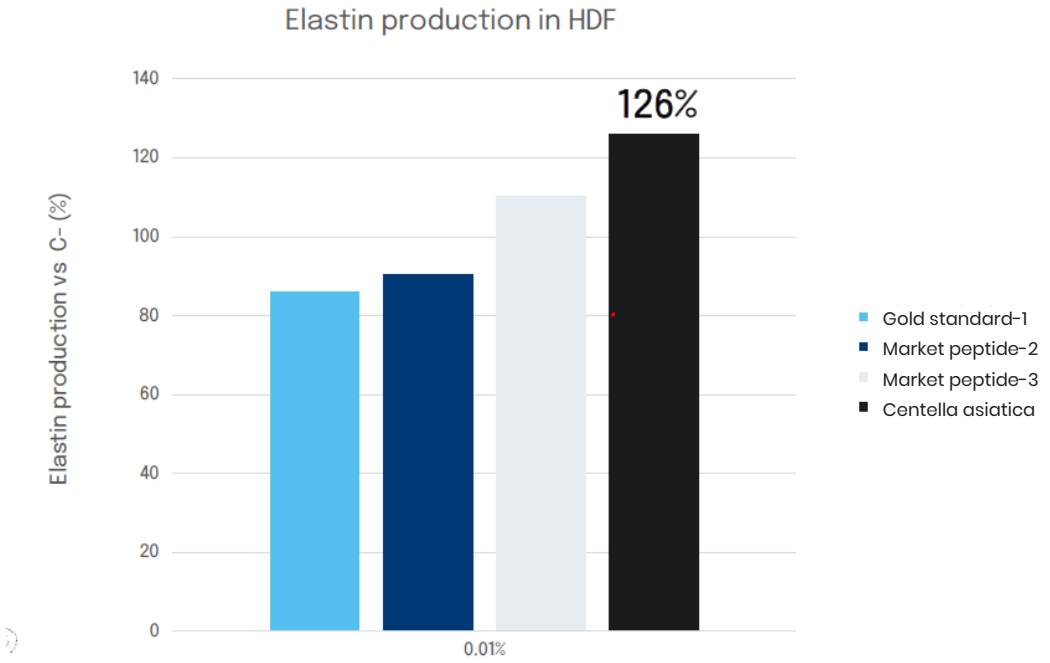
**Efficacy study**

Stimulation of procollagen I in human fibroblasts (HDF)



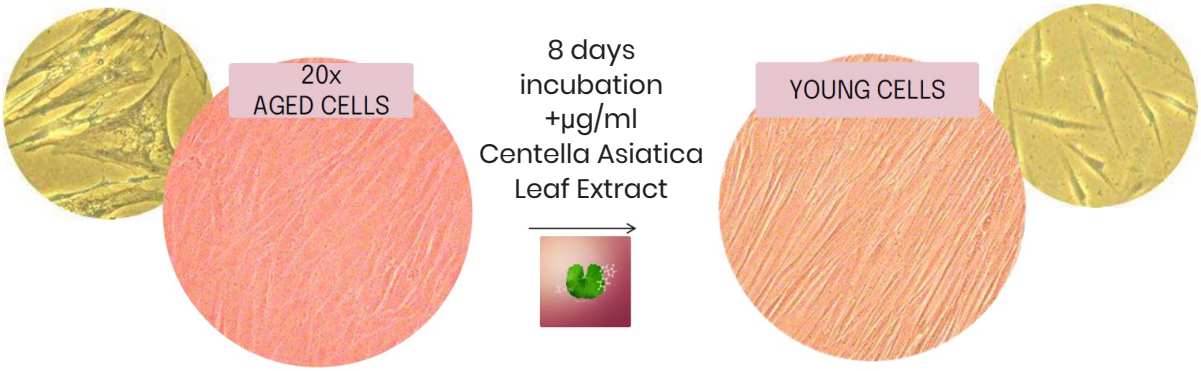

Procollagen I increases up to 134%.
Centella Asiatica increases the levels of procollagen I at a higher level than benchmark.

## Stimulation of elastin in human fibroblasts (HDF)




Elastin increases up to 126%.
Centella Asiatica increases the levels of elastin at a higher level than benchmark.

## Cellular Morphology Reversed
*In vitro* efficacy




A morphology study shows that aged fibroblasts incubated with Centella Asiatica recover a more “young cell” morphology after 8 days, consistent with a partial reversal of senescent phenotype at the cellular level.

In-vivo 1 - Elasticity Rejuvenation Index (ERI)

The ERI represents how closer gets the elasticity of mature skin treated with Centella Asiatica to the young skin elasticity values.

| | | | 28D | | 56D |
|---|---|---|---|---|---|
| Parameter | (55-23) $t_0$ | ($55t_{28}$-23) | % ERI 28d | ($55t_{56}$-23) | % ERI 56d |
| Elasticity (Ur/Uf) | - 0.2009 | - 0.1764 | 12.19% | - 0.1728 | 14% |
| Rejuvenation in years | | | 3.9 | | 4.5 |

28D: 32*12.19%= 3.9 years younger
56D: 32*14%= 4.5 years younger

**20 vol. Reference Group (20-25, av. 23 years old) (One single measurement at the beginning of the study
(*Total age difference between mature (55y) and reference (23y) panels = 32 years)

This table shows that Elasticity Rejuvenation Index (ERI) improvements correspond to ≈3.9 years younger at 28 days and 4.5 years at 56 days on average, with a responder up to 14.6 “elasticity-years” younger.

## *In-vivo 2* - Facial complexion

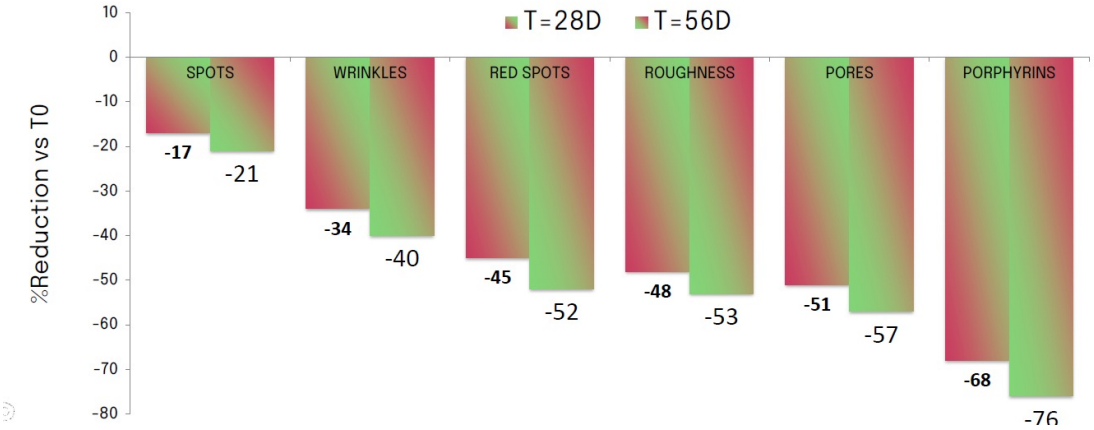
analysis by VISIA®

- Double blind study vs. placebo
- Area of application: face (crow’s feet)
- 2 daily applications
- 6 parameters analyzed: wrinkles, texture (skin roughness), visible spots, red spots, pores & porphyrins*

2% Dosage - 28 days

Facial complexion analysis by VISIA®

GLOBAL IMPROVEMENT OF SKIN APPEARANCE



VISIA® analysis showed reductions in wrinkles, spots, redness, roughness, pores and porphyrins by up to ~50–76% over 56 days.

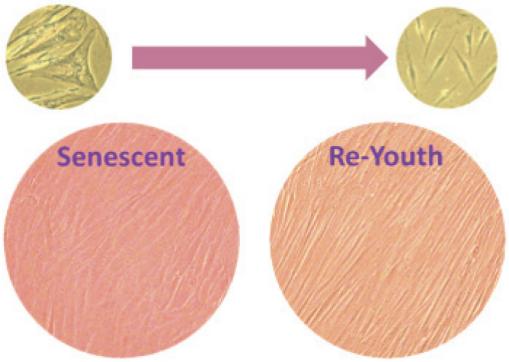
These data together support the idea that Centella exosomes help “reset” aged fibroblasts and ECM towards a younger functional state, which is the practical meaning of skin longevity in a cosmetic context.

In Vitro Efficacy
1. Wound healing and regenerative properties (scratch test)

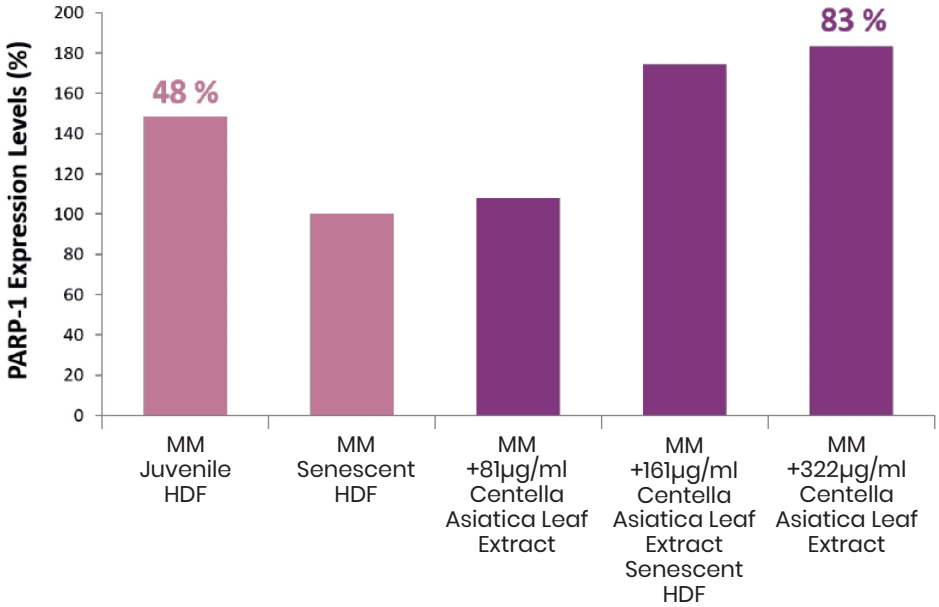

Centella Asiatica Leaf Extract accelerates the healing process up to +72% high compared to baseline conditions.

2. Senescence reversion in human dermal fibroblasts

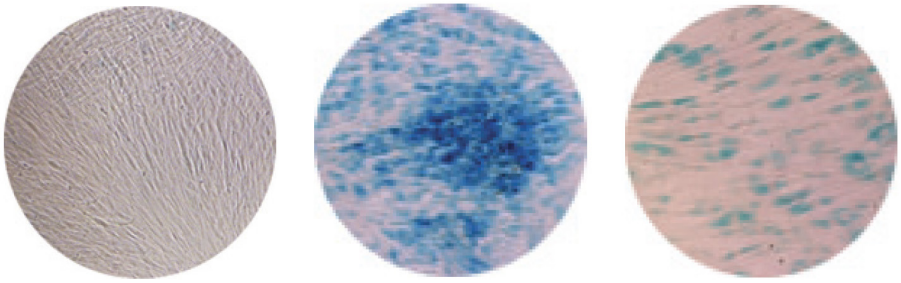
Fibroblast re-shaping




PARP-1: DNA protection enzyme



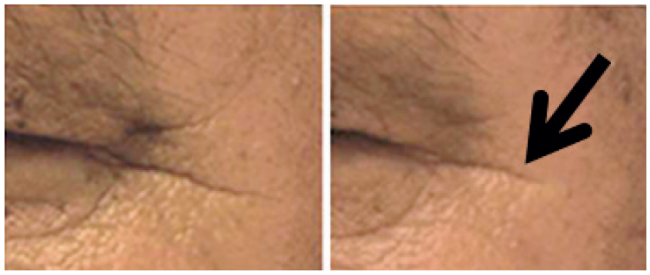
ß-Gal Expression Levels



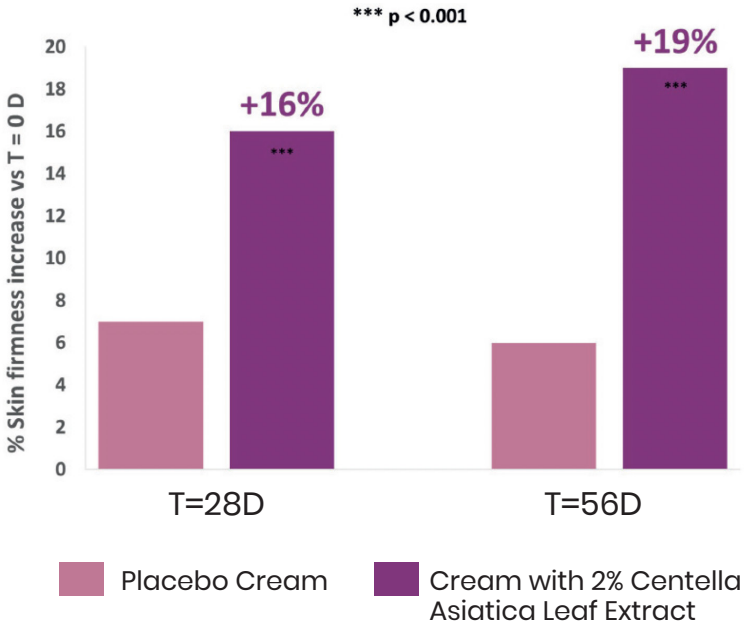
Young HDF | Senescent HDF | Senescent HDF Centella Asiatica Leaf Extract

Up to 83% increases of PARP-1 levels, reaching higher levels than juvenile cells.
Centella Asiatica Leaf Extract can revert the cell senescence and recover the juvenile phenotype.
Up to 41% reduction of ß-Galactosidase levels at the studied doses.

In Vivo Efficacy
1. Evaluation of skin well-ageing effect.



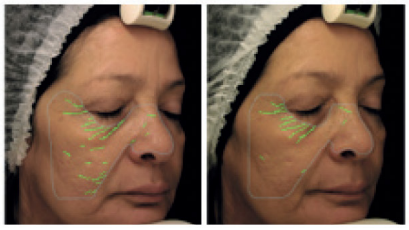
Initial | After 56 days




Up to 42.9% reduction of wrinkle intensity and length progressively and significantly.
Up to 14.6 years younger.

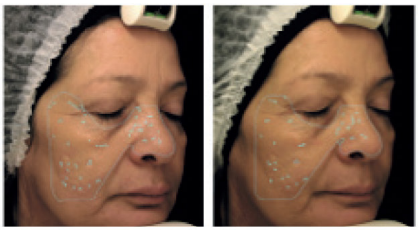
2. Analysis of facial complexion

Wrinkles reduction



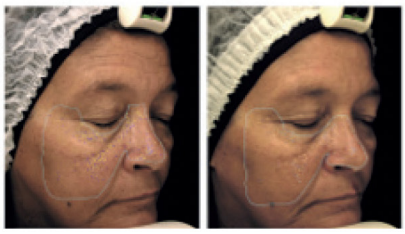
Initial After 56 days

Spots reduction



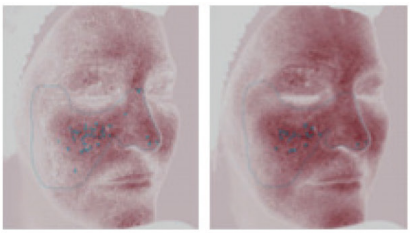
Initial After 56 days

Roughness improvement



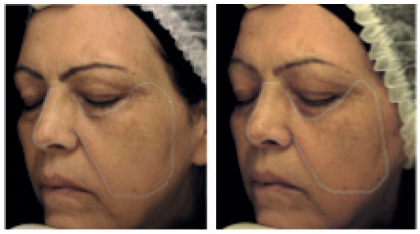
Initial After 56 days

Red spots reduction



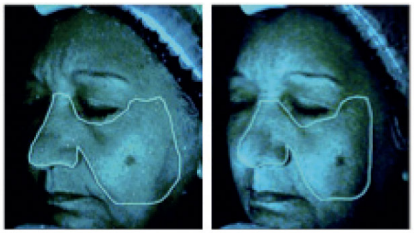
Initial After 56 days

Pores reduction



Initial After 56 days

Porphyrins improvement



Initial After 56 days

Up to 46% & 21% increase in both firmness and elasticity of the skin at 56 days.
Global skin improvement in the 6 parameters analysed.

Links:
Data on file

Cho EG. et al. “Panax ginseng-derived extracellular vesicles facilitate anti-senescence effects in human skin cells.” Cells 2021.

Physalis peruviana ELNs and human dermal fibroblast regeneration (conference/article summarised in (ResearchGate)).

Coriander-derived ELN hydrogel improving wound healing.

Nan L. et al. “Recent advances in dermal fibroblast senescence and skin aging.” Front Pharmacol 2025.

Zhang J. et al. “Aging in the dermis: Fibroblast senescence and its impact on ECM.” Aging Cell 2024.

Chin T. et al. “The role of cellular senescence in skin aging.” NPJ Aging 2023.

## PULLULAN (PULLULAN POLYSACCHARIDE)

Ingredient Claims:

| | |
|---|---|
| Stimulates production of new collagen | Protects skin cells from oxidative damage |
| Skin feels smoother and tighter | Reduces the signs of ageing |

A polysaccharide derived from a fungus that is beneficial in dermal regeneration and capable of stimulating fibroblasts to produce collagen. Pullulan also has antioxidant properties which can help to protect the skin from damage caused by free radicals. Free radicals are unstable molecules that can damage skin cells and contribute to the signs of aging. Pullulan forms a thin film on the surface of the skin, which can help to tighten and firm the skin. This can give the skin a smoother, more youthful appearance.

Sources
https://pubmed.ncbi.nlm.nih.gov/31350941/
https://pubmed.ncbi.nlm.nih.gov/31978478/

## HYDROLYZED DNA - (ORYZA SATIVA POLYDEOXYRIBONUCLEOTIDE (PDRN))

Ingredient Claims:

| | |
|---|---|
| Improves skin texture and smoothness. | Helps reduce pore size by 8.1% in 2 weeks. and number for refined skin appearance. |
| Enhances skin hydration up to 30% and barrier function | Provides antioxidant protection against ROS, reducing them by 34.62% |
| Reduce Melanine production by 43.5% and reduces pigmentation signalling by 30% for a brighter and more even complexion. | Supports wound healing with 11% boosting and tissue regeneration. |
| Boosts dermo-epidermal junction proteins (Laminin-5 by 215%, Collagen XVII by 156%) for firmer, stronger skin. | |

Rice PDRN is a new sustainable vegan innovation in skincare avoiding the controversial concern about using animal such as salmon DNA in humans, Rice PDRN is a DNA-derived skincare ingredient that provides purines and nucleotides, which are natural building blocks that help support the skin's renewal process. By supplying these essential components, it encourages a smoother, more resilient appearance while helping to maintain hydration and elasticity. This gentle yet effective action leaves skin looking revitalised, radiant, and healthy, with improved barrier function and visible suppleness.

What is a PDRN?

Polydeoxyribonucleotide (PDRN) is a mixture of defined DNA fragments (typically 50–1300 kDa) composed of purine and pyrimidine bases, deoxyribose sugar and phosphate groups.

On skin, PDRN has been shown to:

- Provide nucleotides and nucleosides for the DNA salvage pathway → supporting DNA repair and cell proliferation.
- Act as an adenosine A2A receptor agonist, increasing cAMP, reducing NF-κB activity, lowering pro-inflammatory cytokines, and stimulating collagen synthesis.
- Promote angiogenesis, fibroblast activity, ECM production and wound repair, as shown across multiple dermatology studies with injectable and topical PDRN.

DNA content: >2,000 mg/kg; molecular weight distribution ~50–130 kDa (vs 300–1000 kDa typical for salmon PDRN).

Mechanism of action of PDRN in skin longevity & healing:

**DNA salvage pathway – “building blocks” for renewal**

PDRN: **P**oly**D**eoxy**R**ibo**N**ucleotide helps:

- provide purines and pyrimidine rings for the “salvage pathway”
- generating nucleotides and nucleosides to contribute to DNA formation
- cell proliferation, leading to a faster tissue regeneration and wound healing

1. This shows PDRN fragments entering cells and being broken down to nucleosides and bases.

2. These fragments feed into the DNA salvage pathway, which recycles bases to synthesize new DNA.

3. In keratinocytes and fibroblasts, this supports cell division and replacement of damaged cells, enhancing epidermal turnover and dermal matrix maintenance.

From a skin longevity viewpoint, this means:

- Better capacity to repair everyday DNA damage (UV, pollution, oxidative stress).
- Maintenance of a healthy pool of proliferative cells, avoiding premature functional decline.

**Adenosine A2A receptor activation**

PDRN is binding the A2A receptor, increasing cAMP, inhibiting NF-κB and downstream inflammatory mediators, while enhancing collagen gene expression and MMP inhibition.

Practical consequences for healing and longevity:

- Anti-inflammatory: reduced IL-1β, IL-6, TNF-α and COX-2 expression; helps control chronic low-grade inflammation that accelerates aging.
- Pro-regenerative: increased growth factors and ECM proteins (collagen, fibronectin, laminins) and improved angiogenesis; crucial for wound closure and post-procedure recovery.

Where does it come from?

Traditionally, cosmetic and medical PDRN is sourced from salmon or trout DNA. Plant-derived (“green”) PDRN is a newer, vegan alternative in which the same class of DNA fragments is extracted from botanical sources such as rice bran, ginseng roots or rose petals.

PDRN Salmon

Origin: Salmon’s semen or testis
Process: Raises fishes > extracts semen or testis from salmons
But: Derived from living organism
No avaliable vegan claim

Green PDRN

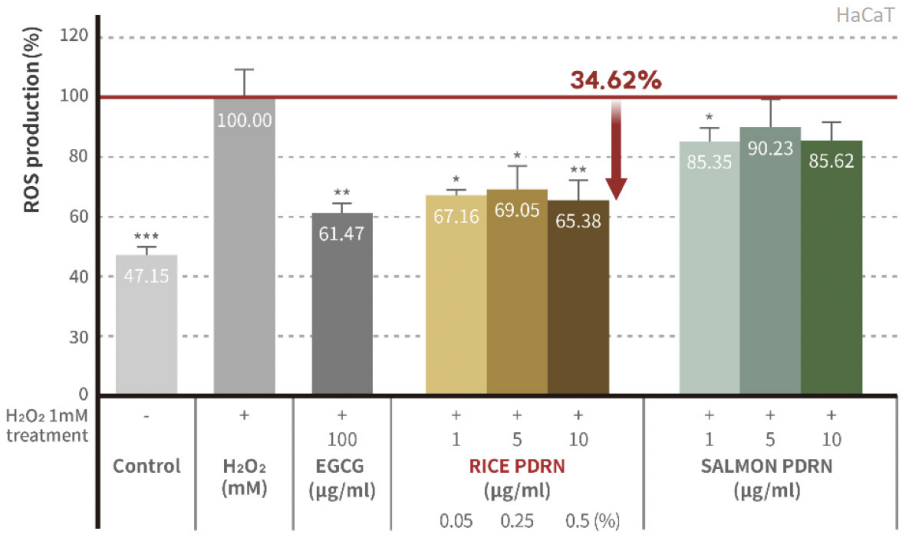
Origin: Plants
Process: Typical method for each type of raw material
So: Vegan/Cruelty free
Customisation available

Advantages of the green PDRN

- Vegan and cruelty-free: derived from plant cell cultures or agricultural by-products (e.g. rice bran).

- No risk of animal pathogens and better alignment with religious/ethical requirements.

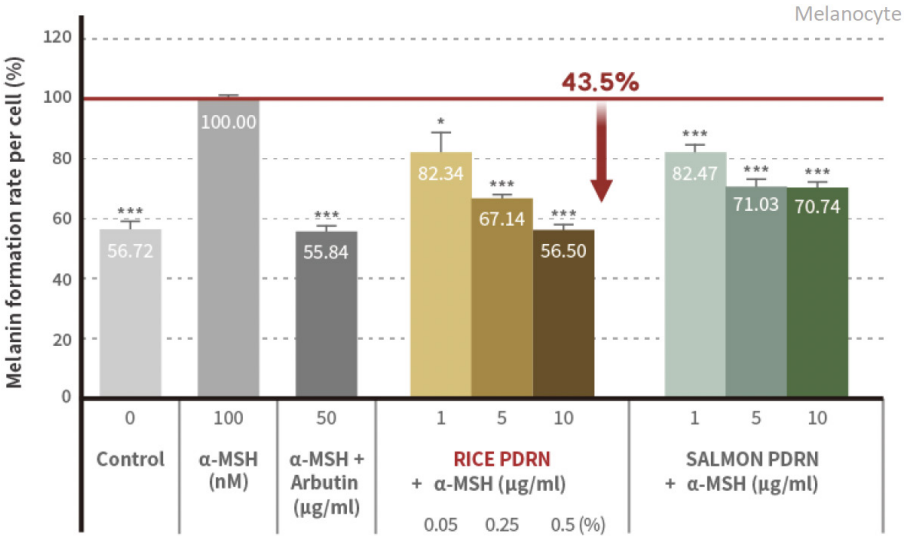
Anti-oxidant
(ROS Production)



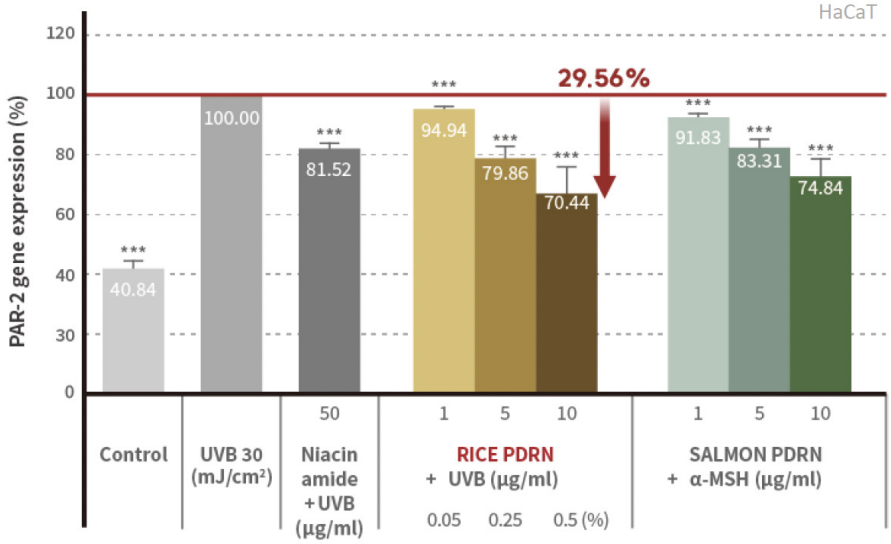

Rice PDRN reduced reactive oxygen species (ROS) by ~34.6% versus control, comparable or superior to salmon PDRN at tested levels.

This supports protection against oxidative stress, a key driver of DNA damage and cellular ageing.

Skin brightening
(Melanin formation)



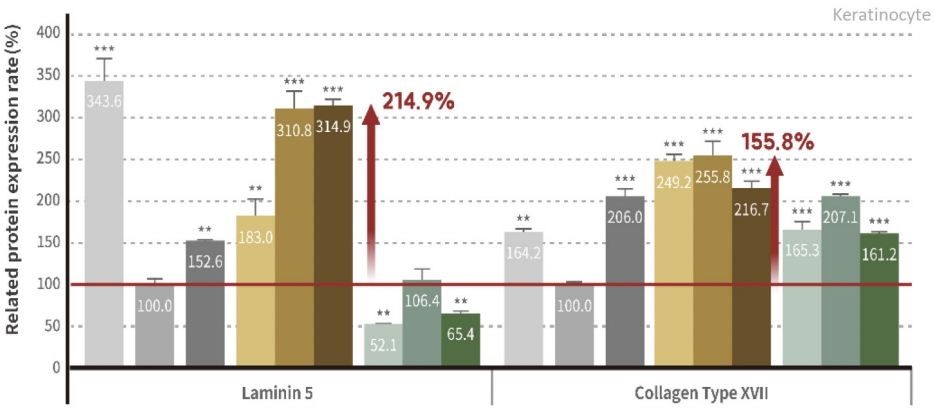

Skin brightening
(PAR-2 mRNA)

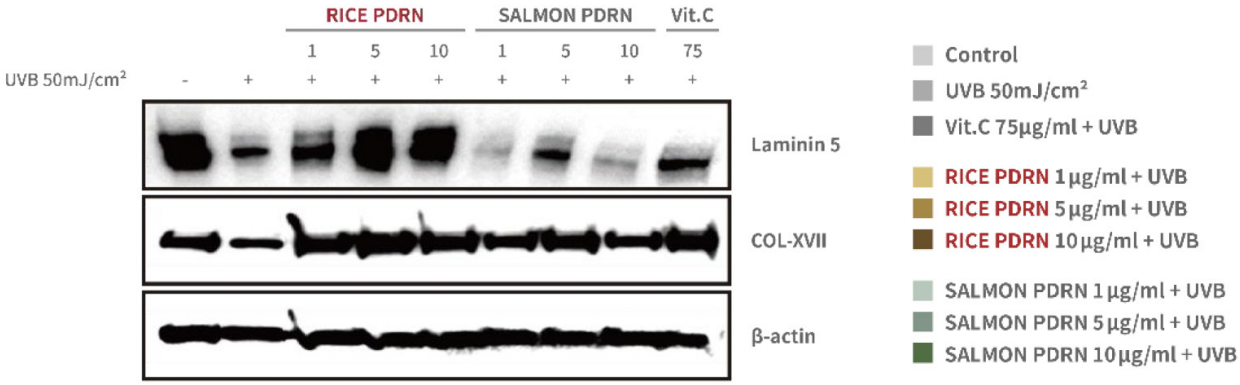


Wound healing & Regeneration:

- Scratch assay in fibroblasts shows that Rice PDRN improved wound closure by approximately 11% vs control, again comparable to or better than salmon.

DEJ Strenghtening (Laminin5, Collagen type XVII)




**Dermal–epidermal junction (DEJ) strengthening:**

The Western blot and bar chart show that Rice PDRN at cosmetic use levels increased:

- Laminin-5 expression by about 215% vs control.
- Collagen XVII expression by about 156% vs control.

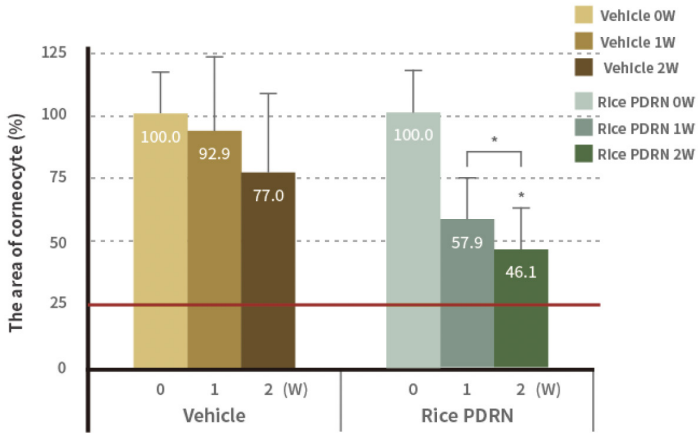
So PDRN boosts DEJ proteins (Laminin-5 by 215%, Collagen XVII by 156%) for firmer, stronger skin as DEJ strengthening is key for:

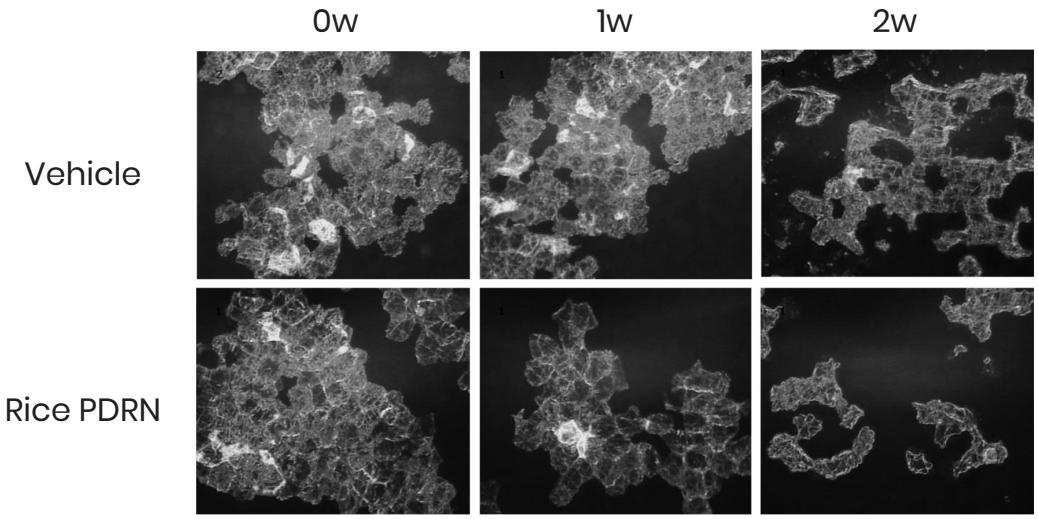
- Firmness and resistance to shear forces.
- Better nutrient and signal exchange between epidermis and dermis.
- Long-term mechanical longevity of skin.

Clinical tests:

- 1% Rice PDRN serum vs vehicle
- 3 female subjects per group, mean age ≈ 34 years
- Application twice daily for 1 and 2 weeks

The area (%) of corneocyte

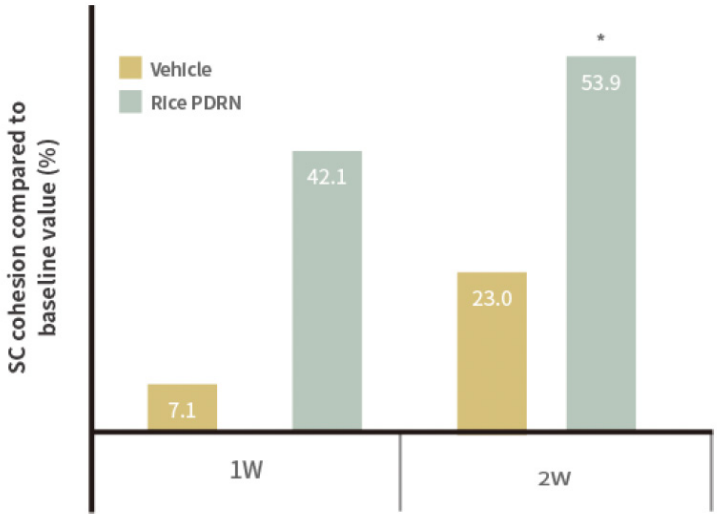



Tape-stripping images and quantification show a reduction in corneocyte area vs baseline and vehicle, indicating finer, more uniform exfoliation (“glass skin” texture).

So, Rice PDRN improved skin texture and smoothness.

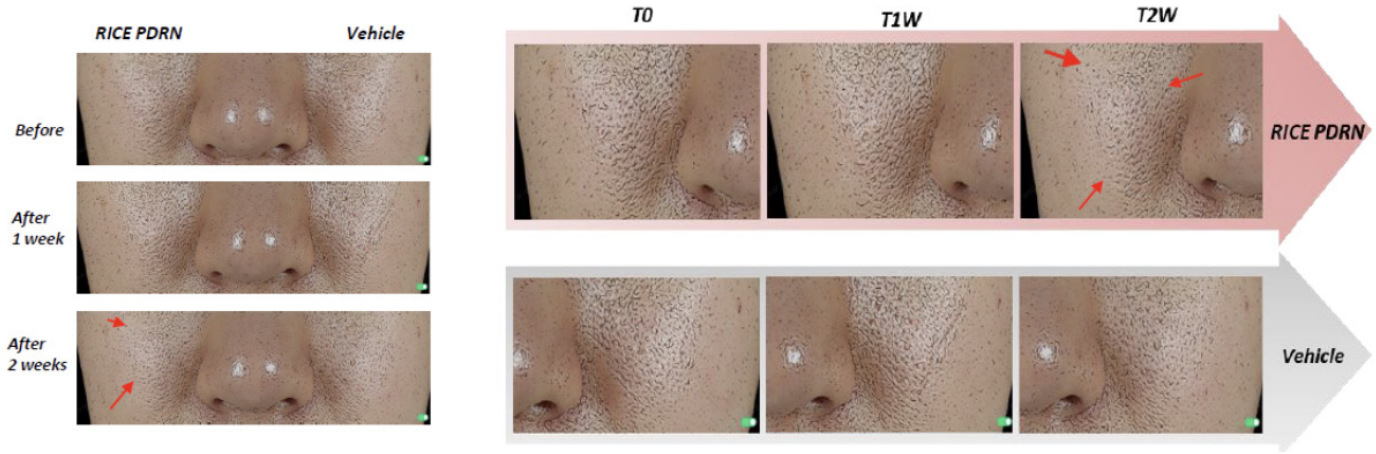
The change rate (%) compared to baseline value



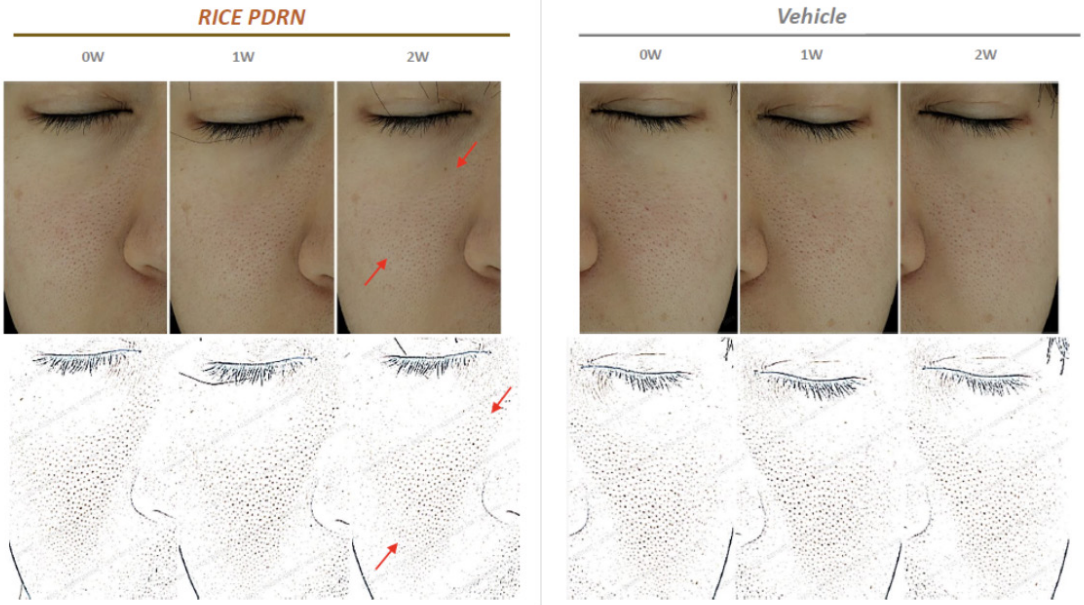
Skin texture by line parameter analysis

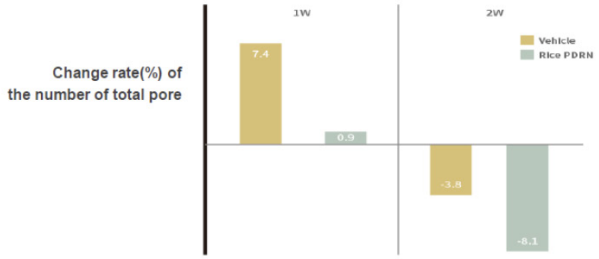
Skin texture is analyzed by measuring the line parameters images from the reflection of parallel-polarized light from skin surface on each angle. On smoother skin, parallel-polarized light is less reflected and makes no lines.

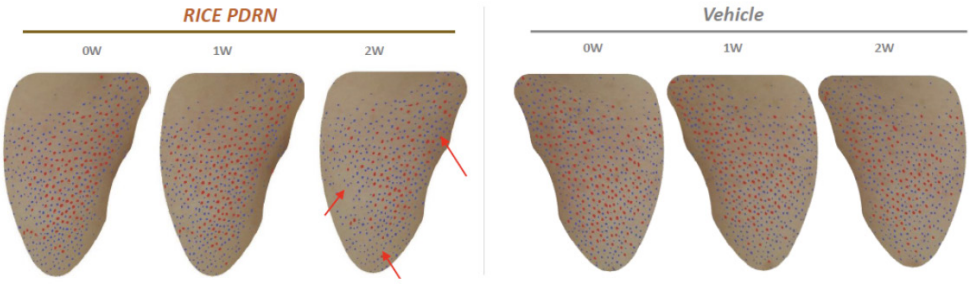
- After 2 weeks, the lines on skin appliced with Rice PDRN shortened or eliminated.




Pore care



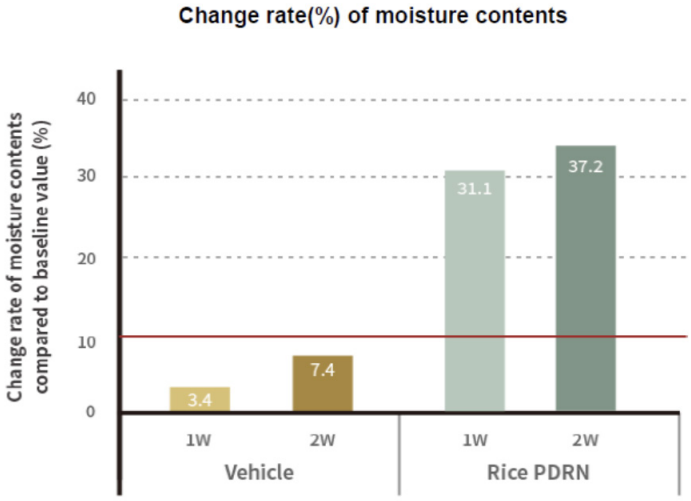
Pore imaging shows visible reduction in pore visibility with Rice PDRN over 2 weeks, whereas vehicle changes are minimal.

This study shows a pore size reduced by 8.1% in 2 weeks and a reduction in pore number.

Pore imaging shows visible reduction in pore visibility with Rice PDRN over 2 weeks, whereas vehicle changes are minimal.

This study shows a pore size reduced by 8.1% in 2 weeks and a reduction in pore number.

Skin hydration




Corneometer data show +31–37% increase in skin hydration at 1–2 weeks vs baseline with Rice PDRN, compared with ~3–7% for vehicle.

So, this study shows up to 30% hydration improvement and better barrier function, using PDRN.

Links:
Data on file

Khan A, Wang G. Polydeoxyribonucleotide: A promising skin anti-aging agent. 2022.

Park S et al. Clinical Applications, Pharmacological Effects, Molecular Mechanisms of PDRN in Skin Disorders. 2025.

Akaberi SM et al. PDRN in Skincare and Cosmetics: Therapeutic Potential in Dermatological Applications. 2025.

Lebiedzińska J. Polynucleotides and Polydeoxyribonucleotides in Dermatology – A Narrative Review. 2025.

Lee KS et al. Impact of PDRN on Wound Healing (reviewed in 2025 International Journal of Surgery review).

Kim E et al. Safety Validation of Plant-Derived Materials for Skin Applications. Cosmetics 2025.

Cosmacon. Rice PDRN – The Vegan Skin Booster for Regeneration and Protection.

## ACETYL HEXAPEPTIDE-8

Ingredient claims:

| | |
|---|---|
| Up to 31% faster relaxation of facial muscles | Reduced appearance of fine lines by up to 14.7% |
| Boosts type 1 collagen by up to 25.9% in aged skin | Skin looks 13.8% more plump |
| Enhances synthesis of new collagen by 53.7% | 1.5% reduction in skin sagginess |
| Wrinkle area reduced by 11% in 5 days | Facial muscles up to 11.1% more relaxed |
| Crow's feet appear 5.9% smoother | |

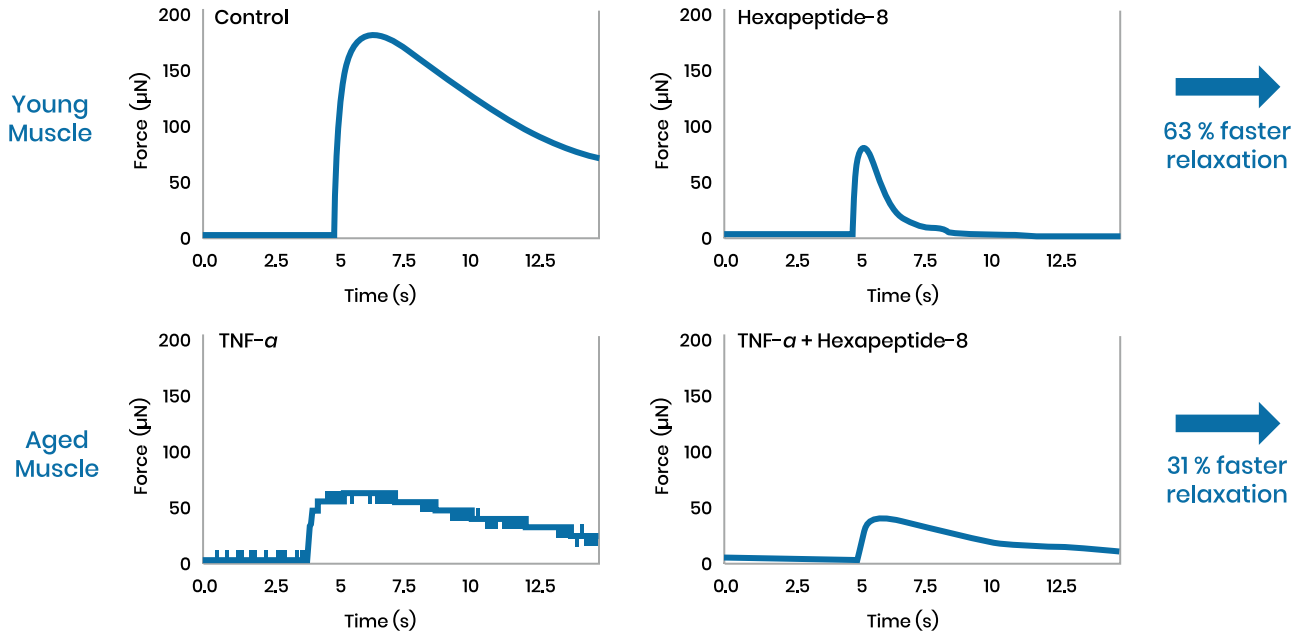
Commonly referred to as "Botox in a jar" because it inhibits the release of neurotransmitters and relaxes the facial muscles, this relaxation of facial muscles in turn reduces the appearance of expression lines and wrinkles. Acetyl Hexapeptide-8 is a peptide compound that is used to reduce the appearance of wrinkles brought on by repeated facial expressions. It is composed of chains of amino acids known as peptides. Fine lines and wrinkles around the eyes and mouth typically form due to repeated facial expressions (such as smiling, frowning, or furrowing the brow in deep concentration or frustration). Acetyl Hexapeptide-8 can temporarily remove the wrinkles by intercepting messages from the brain to facial muscles, thereby preventing muscle contractions that can lead to wrinkles.

In addition to reducing the appearance of expression lines, Acetyl Hexapeptide-8 can also improve the texture of the skin. It stimulates collagen production, which helps to firm and tighten the skin, giving it a smoother and more youthful appearance.

Skin hydration also improves with Acetyl Hexapeptide-8 application. It increases the production of hyaluronic acid, which is a natural moisturiser that helps to keep the skin hydrated and plump.

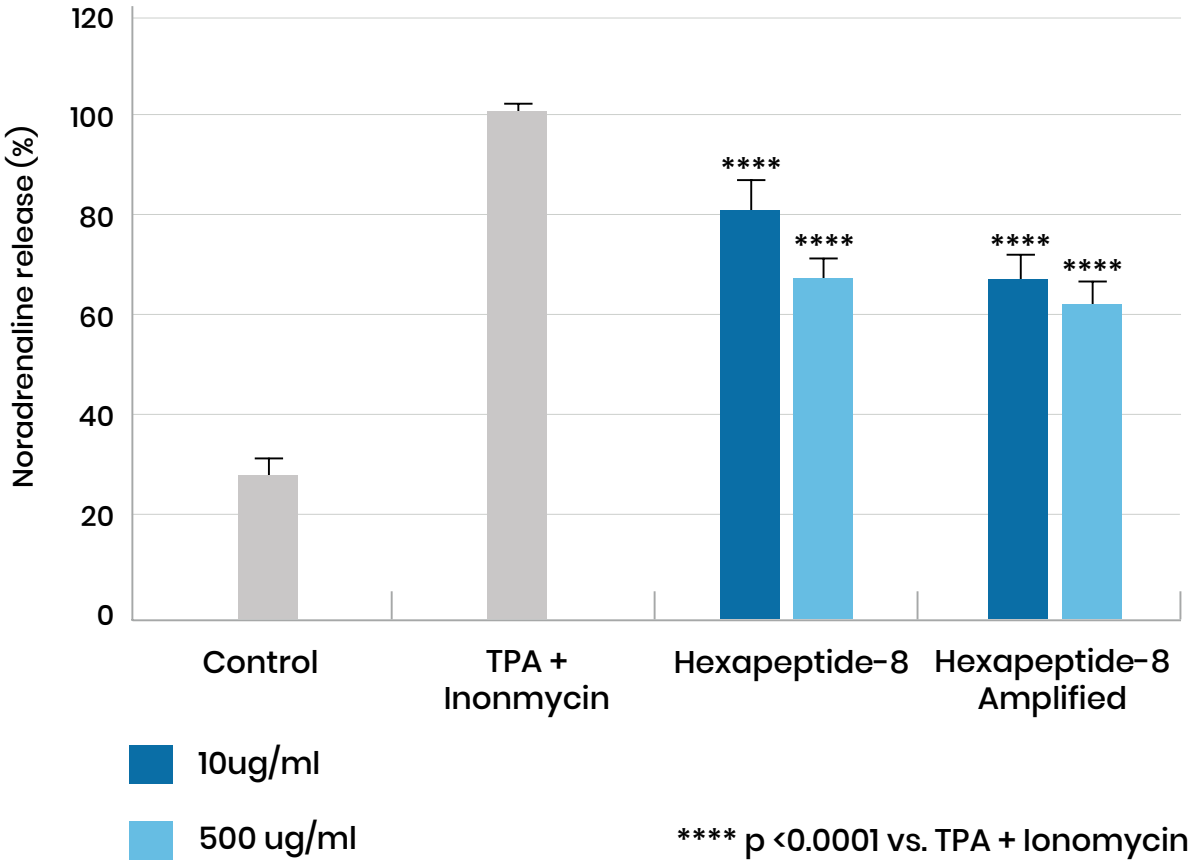
Reduced muscle contraction in 3D bioprinted muscles in both young and aged muscle. Faster muscle relaxation in both groups.

TPA + Ionomycin= calcium binding agent



The peptide helped decrease the relaxation half-time of young and aged muscles by 63% and 31%, respectively.

The peptide reduced the strength of muscle contraction, while also providing a faster muscle relaxation, helping to recover the skin appearance after facial expressions.

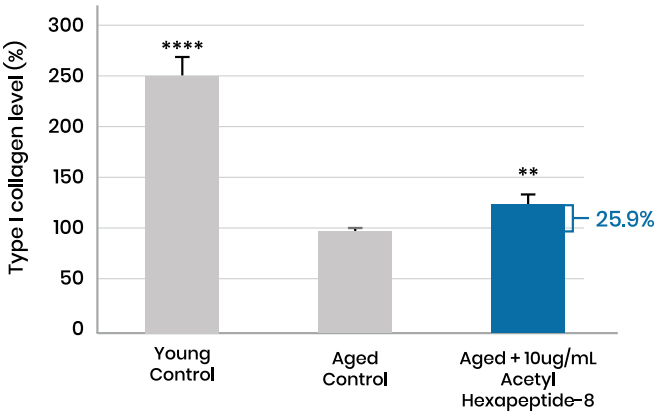



Collagen boosting in aged conditions

This test was performed to evaluate the ability of the peptide to induce type I collagen synthesis even under ageing conditions.

Replicative senescence was induced in human dermal fibroblasts while these were treated with 10µg/ml Hexapeptide-8 peptide or were left untreated control underwent half of the passages of the aged non-treated control.
Type I collagen levels were quantified by alphaLISA assay, and ß-galactosidase staining was performed to ensure the state of senescence of the culture.
ß-galactosidase is an enzyme considered a biomarker of senescence. When cells are treated with the substrate of galactosidase previously linked to a dye, if galactosidase is present and yields an insoluble coloured compound that stains the cells in blue colour. Therefore, the higher the number of senescent cells, the more blue colour in the images.

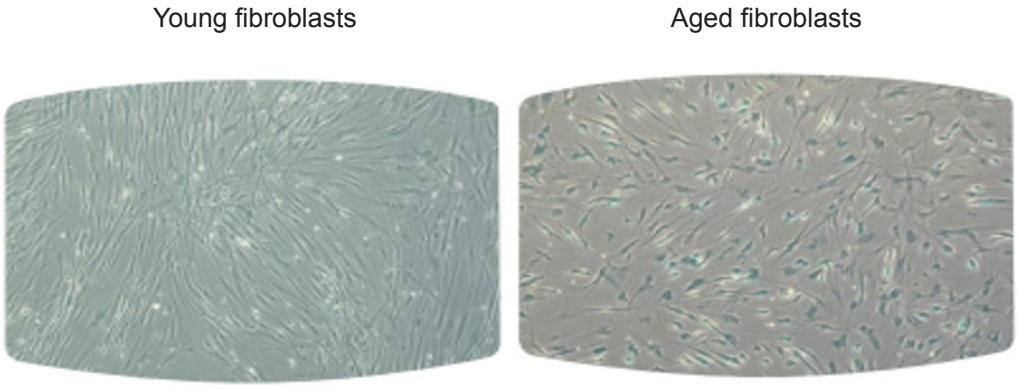
**Collagen boosting in aged conditions**




25.9% higher type I collagen levels even under aging conditions

Control non-treated cells
vs. Aged control: **p<0.01 / ****p<0.0001

Senescence marker (ß-galactosidase)




Human fibroblasts stained with ß-galactosidase (in blue), a biomarker to identify senescent cells.

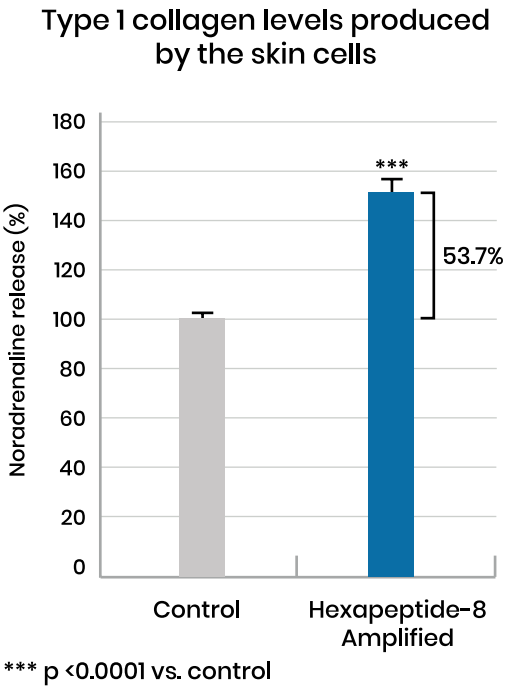
Increase in Type 1 collagen production

This test was performed to evaluate the ability of Acetyl Hexapeptide 8 to enhance the production of new collagen by non-senescent skin cells.

Human dermal fibroblasts co-cultured with human keratinocytes were incubated with 0.5µ/ml Hexapeptide-8 for 48hr or were left with only the medium as a control.

Then, the protein levels of type I collagen were evaluated by using an alphaLISA assay.

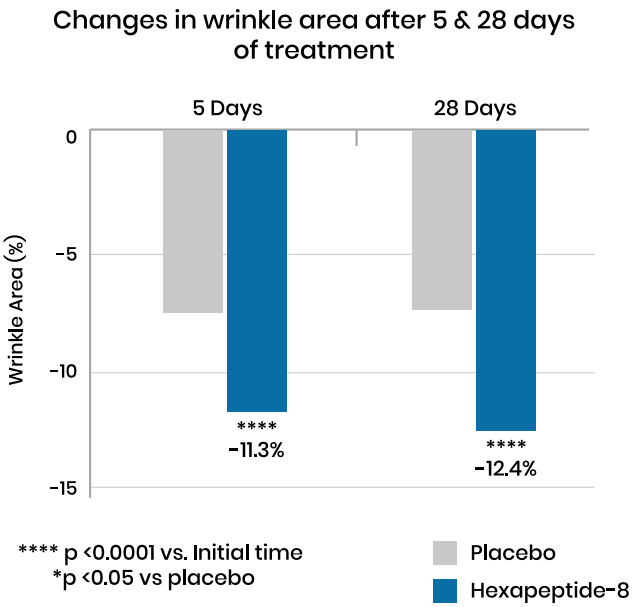
A notable increase in the level of new type 1 collagen was found after the treatment with Acetyl Hexapeptide 8. It has the ability to enhance the synthesis of new collagen by 53.7%.

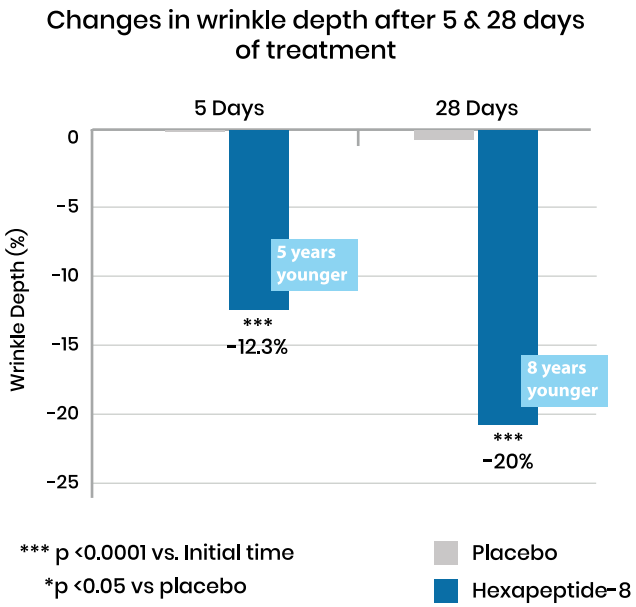



Improving the appearance of expression wrinkles

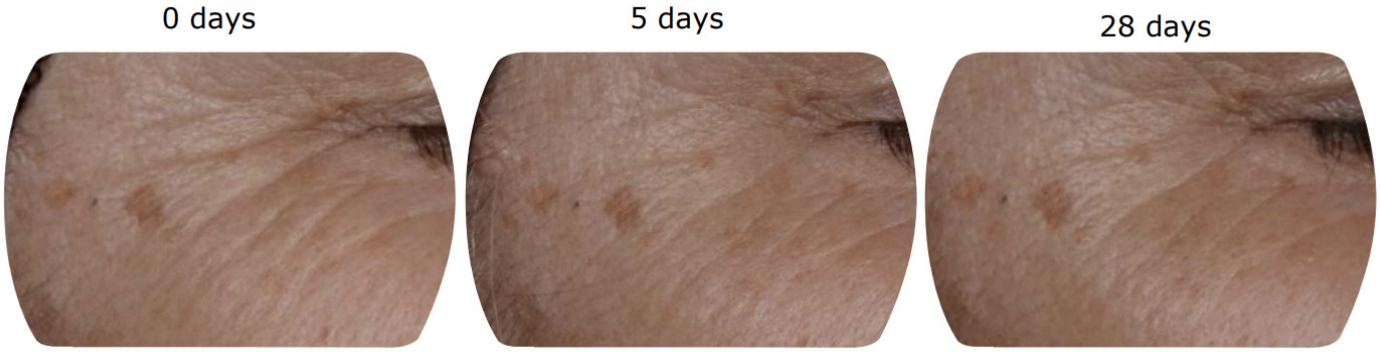
In-Vivo Efficacy
The aim of this study was to evaluate the ability of Acetyl Hexapeptide 8 to minimise expression wrinkles.

Two panels of 41 and 40 female volunteers between 34 and 60 years old applied either a cream containing 2% or 5% Acetyl Hexapeptide 8 solution on half face and a placebo cream on the other half, twice a day for 28 days.




After only 5 days the area (tested at 2%) and depth (tested at 5%) of wrinkles decreased by an average of 11.3% and 12.3%, respectively.

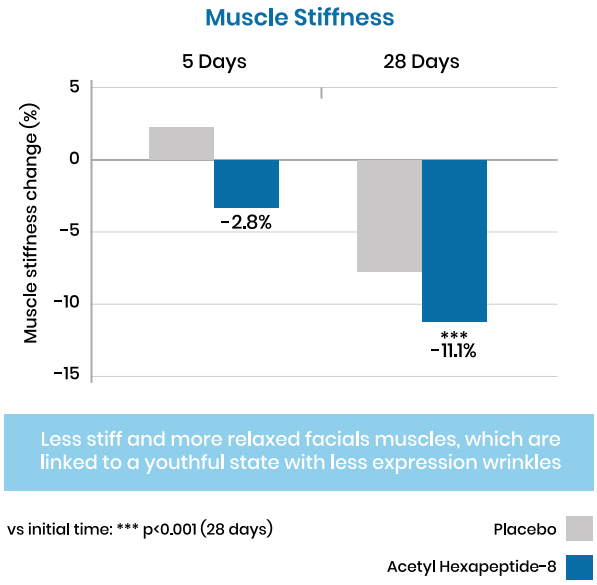



The ability of Acetyl Hexapeptide 8 to recover and relax the skin appearance after facial expressions was assessed by evaluating muscle stiffness and expression wrinkles after smiling.

Muscle Stiffness

41 female volunteers between 35 & 59 years old applied a cream containing 2% Acetyl Hexapeptide 8 solution on half face and a placebo cream on the other half, twice a day for 28 days.

The stiffness of facial muscles, which increases with ageing and reflects the loss in the capacity to relax after a contraction, was measured by myotonometry on the masseter muscle.



Relaxation of facial expressions

43 female volunteers between 35 & 60 years old applied either a cream containing 2% Acetyl Hexapeptide 8 solution or a placebo cream on the whole face, twice a day for 28 days. The reduction in skin roughness was analyzed by means of 3D microtopography imaging system based on fringe projection (PRIMOS) 60 seconds after relaxing smiling facial expressions. The same evaluation was performed before and after 28 days of treatment.

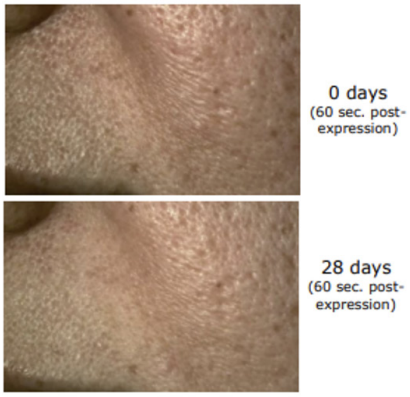

Decrease of roughness (%) of the evolution between smile and post-smile:

Crow's Feet
-5.9% roughness
p<0.1 (vs initial time)

Placebo: +4.81% roughness

Nasogenian fold
-7.4% roughness
p<0.05 (vs initial time)

Placebo: -0.7% roughness


Images of the crow's feet and nasogenian fold of two different volunteers 60 seconds after smiling.

Improved post-expression relaxtion, so you won't stop smiling.

Multi-level improvement in tissue functionality

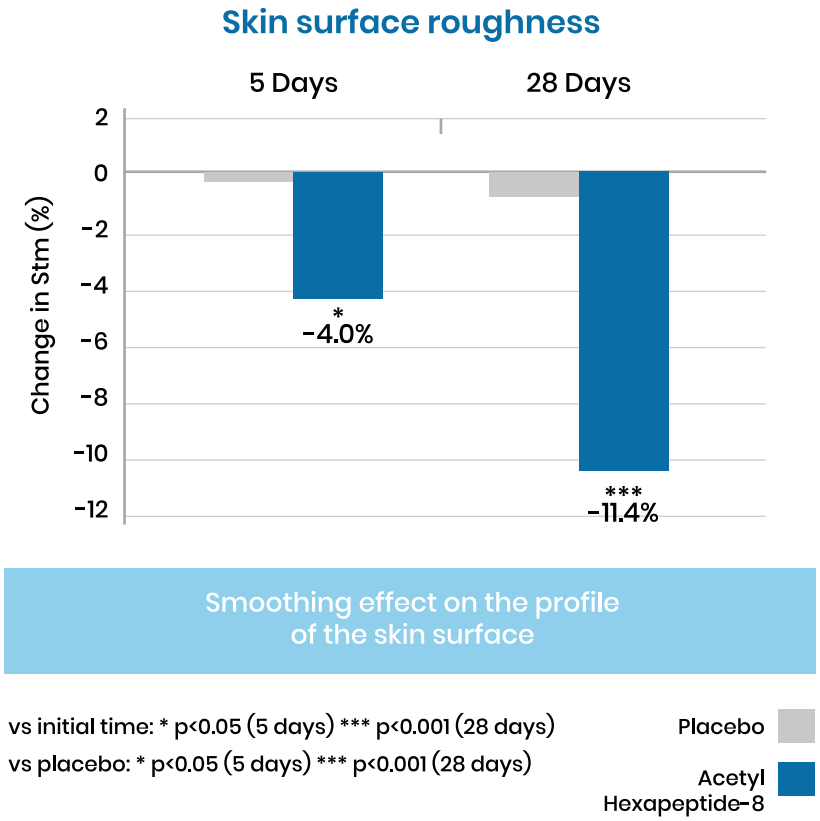
The multifunctionality of Acetyl Hexapeptide 8 was evaluated in this complete clinical study.

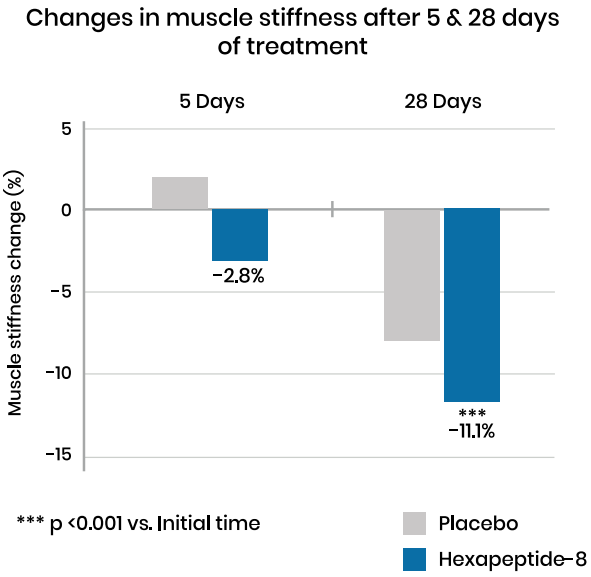
Two panels of 41 and 40 female volunteers between 35 and 60 years old applied a cream containing 2% Acetyl Hexapeptide 8 solution on half face an a placebo cream on the other half, twice a day for 28 days.

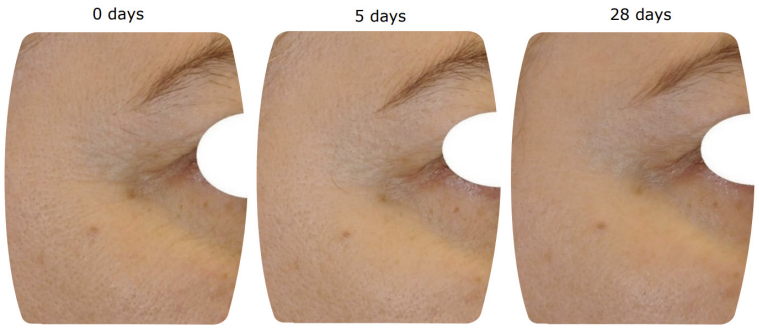
Different parameters related to a better and younger-looking skin were evaluated at different time points during the treatment.

Skin surface roughness

The homogeneity of the skin was assessed by measuring the skin surface roughness by means of 3D microtopography imaging system based on fringe projection (PRIMOS). The change in the average maxium height (Stm) of the skin profile, which corresponds to the average of the vertical distance between the 5 highest and 5 lowest points, was calculated.



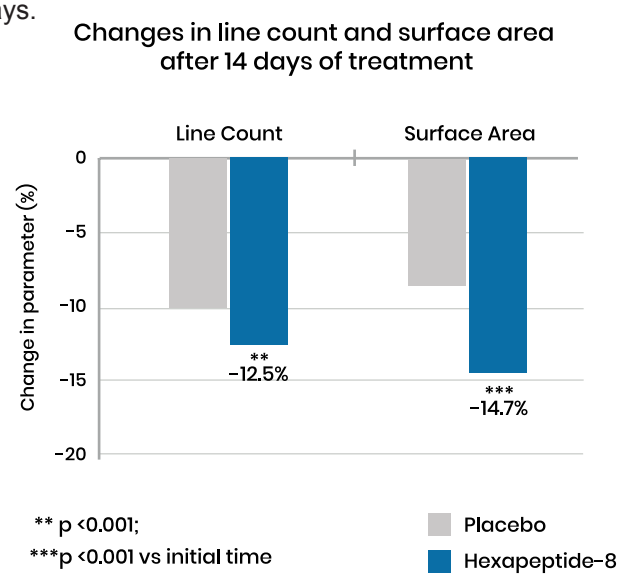



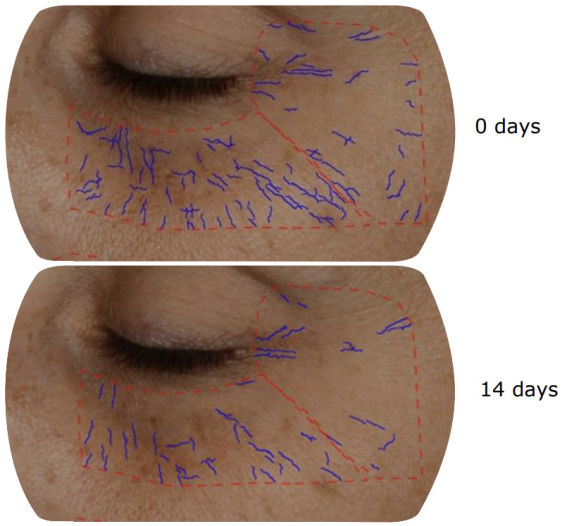




Less stiff and more relaxed facial muscles, which are linked to a youthful state with less expression wrinkles.

Fine lines

The presence of fine lines in the skin surface was measured on the crow's feet area and underneath the eye, after 14 days.

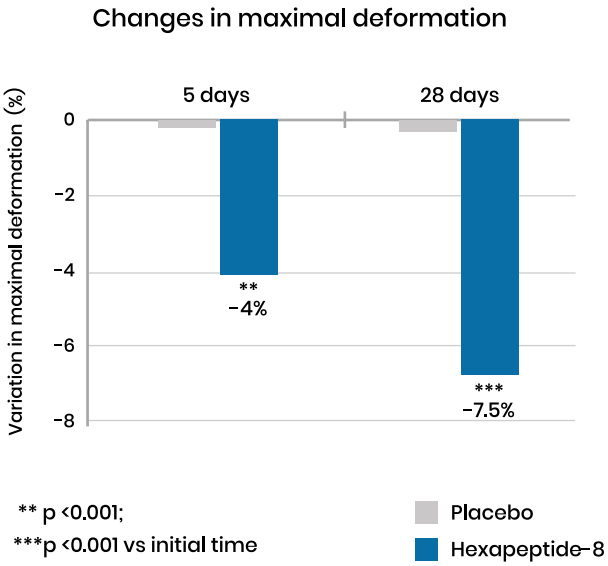


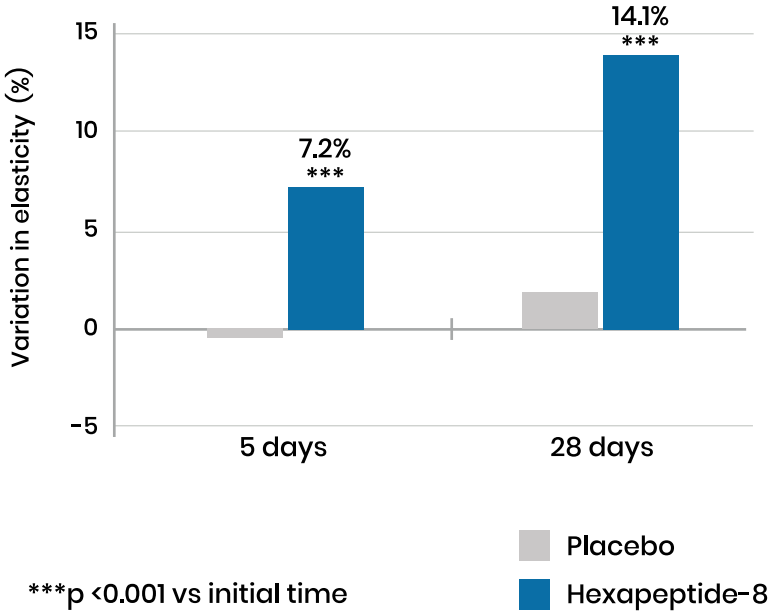

Global reduction of visible fine lines.

Firmness and elasticity

Maximal deformation (R0): represents the passive behaviour of the skin when a pulling force is applied. It is inversely related to firmness.



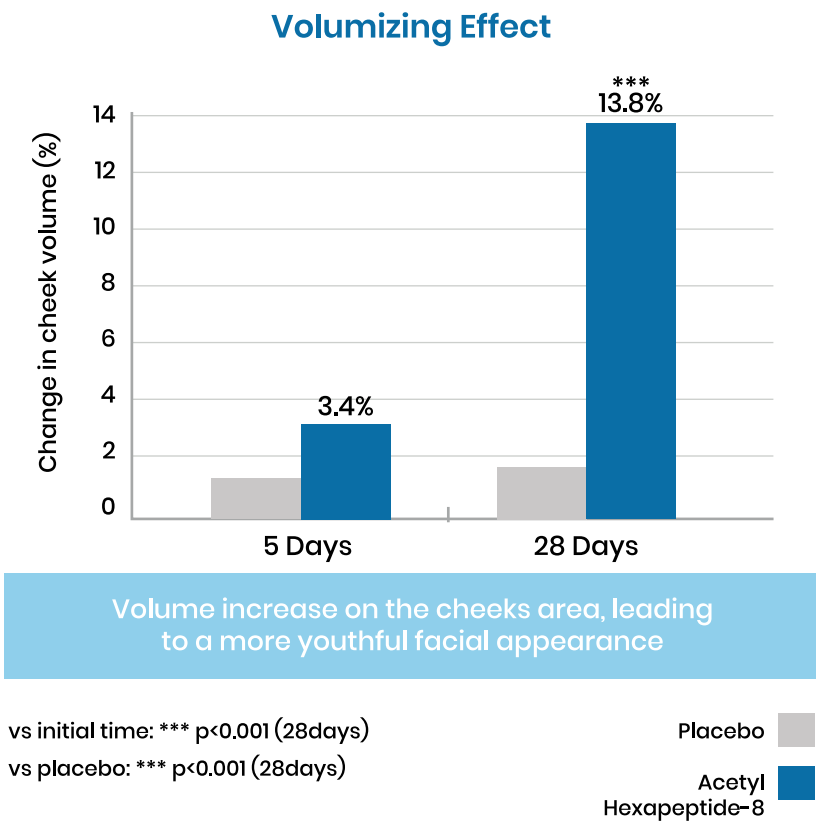

Elasticity (R2): gross elasticity of the skin. It corresponds to how easily the skin returns to its original state after releasing a suction force.




Increase in firmness and elasticity for a tenser effect.

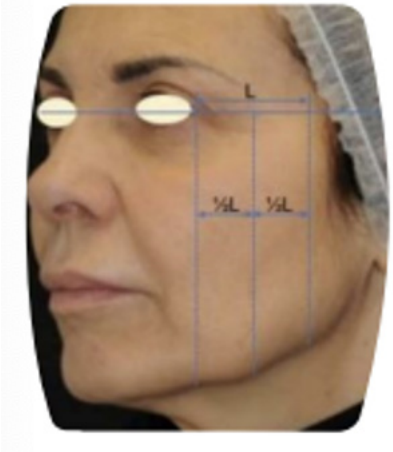
Volumising effect

Changes in facial volume were evaluated on the cheeks by means of an image analysis involving the measurement of the distance between the cheekbone profile and a line passing vertically through the ear. A decrease in cheek distances (mm) corresponds to an increase in volume (%).



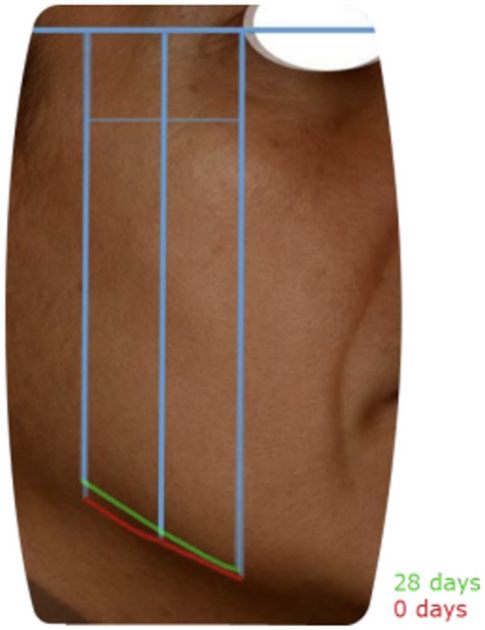

Lifting effect

An image analysis was carried out in order to determine the lifting effect of the ingredient. The analysis consisted of drawing 3 vertical lines and analyzing the lines by means of a specific software as reported in the image below.

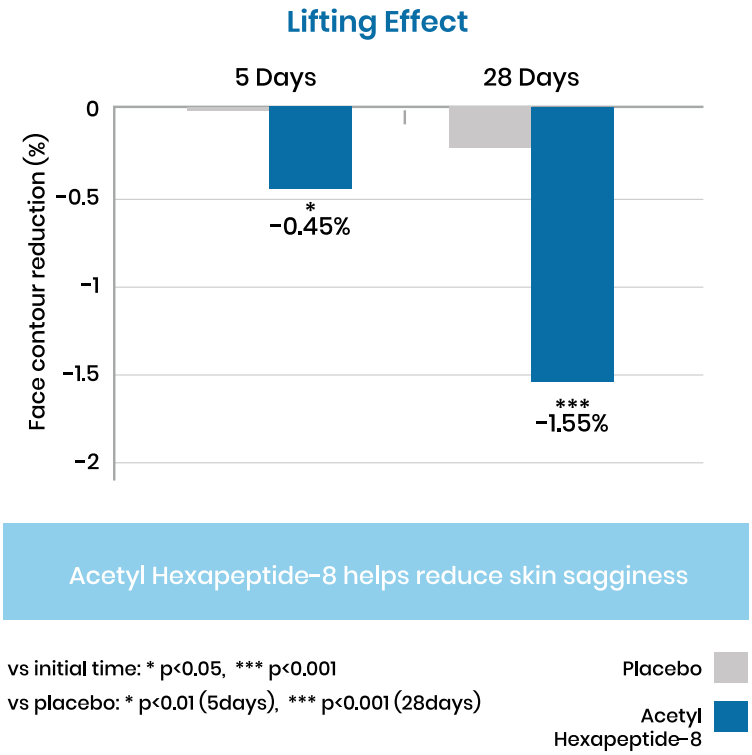


The first vertical line is drawn at the end of the eye, the third one is drawn at “the end of the face” where the sagging ends, and the second one is drawn in the middle of the distance between the first and third vertical lines.
The three vertical lines are drawn along the skin sagging on the face profile and they should cover the whole sagging in order to evaluate the tensor effect.

The shorter the distance of the 3 vertical lines, the bigger the lifting effect.

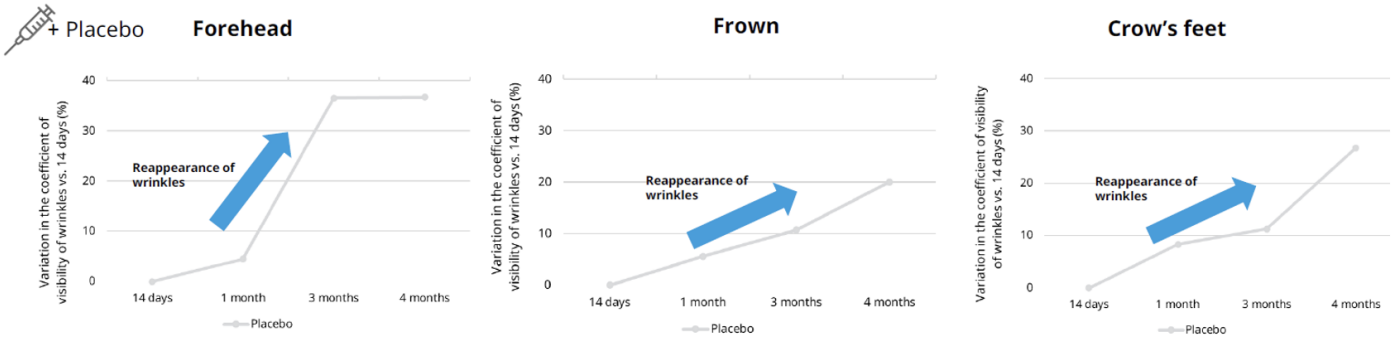



Superimposed before and after images of a volunteer, showing a visible lifting effect at the end of the treatment.



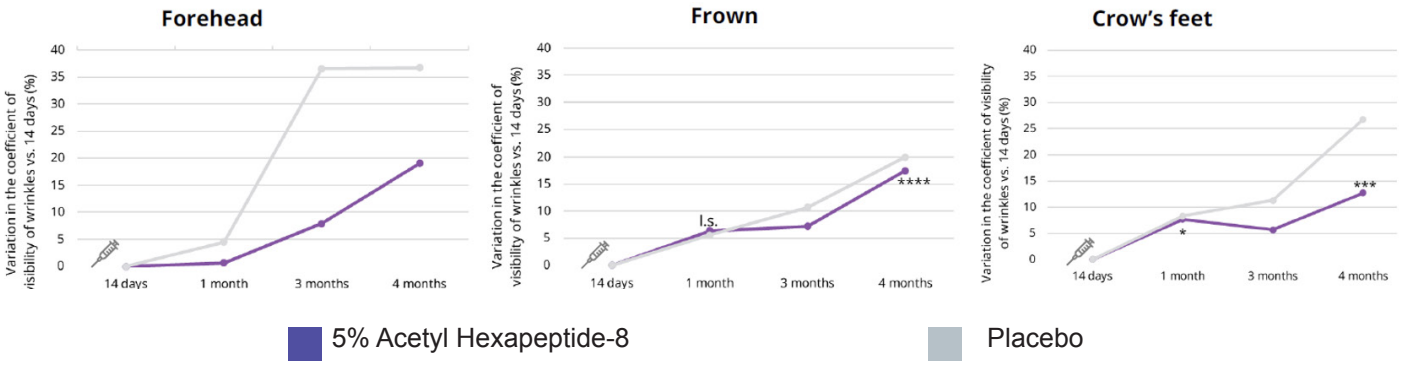

Extending the effect of Botox Injections

- 45 female and male Caucasian volunteers
- 35-60 years old
- 50 UI Botulinum toxin type A injection treatment to all volunteers in crow's feet, frown and forehead area
- Cream with 5% Acetyl Hexapeptide-8 solution or placebo cream on the whole face twice daily, for 4 months
- Coefficient of visibility of wrinkles
- Skin roughness
- Wrinkle length

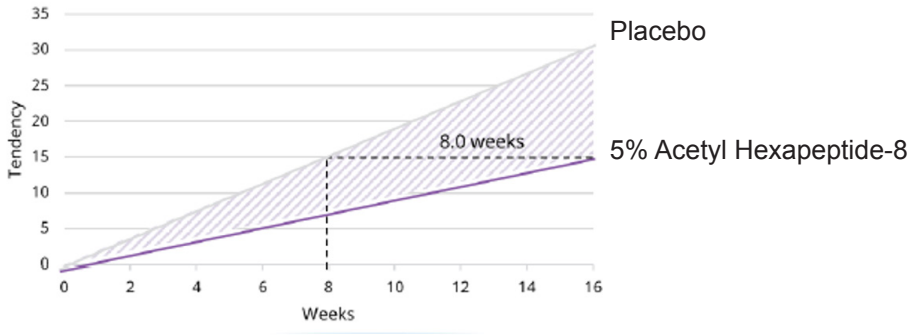



The effect of botunlinum toxin treatment starts to wear off after 28 days.
After 4 months, 87% of volunteers could no longer notice the effect of the botulinum toxin injections.

Coefficient of visibility of wrinkles vs 14 days




5% Acetyl Hexapeptide-8 Placebo




Placebo

5% Acetyl Hexapeptide-8

Helping delay the wear off effect of botulinum toxin by 8 weeks on average.

Delayed reappearance of forehead wrinkles with surprise expression

Botulinum toxin injection + Placebo


Male volunteer 6, 35 years old

Botulinum toxin injection + Acetyl Hexapeptide-8


Male volunteer 32, 44 years old

Delayed reappearance of forehead wrinkles with concerned expression

Botulinum toxin injection + Placebo

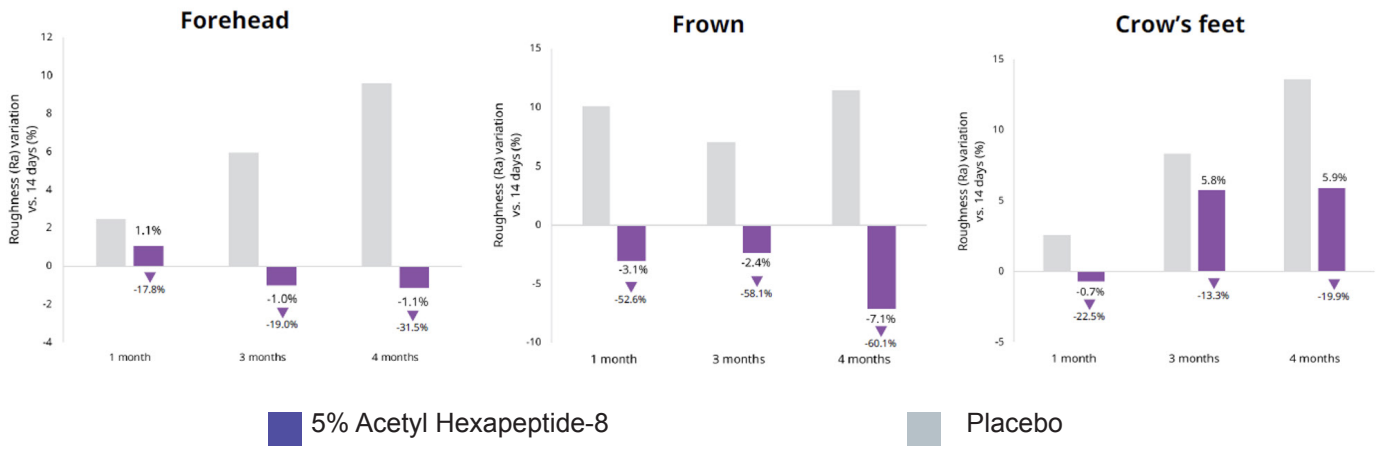

Male volunteer 6, 35 years old

Botulinum toxin injection + Acetyl Hexapeptide-8

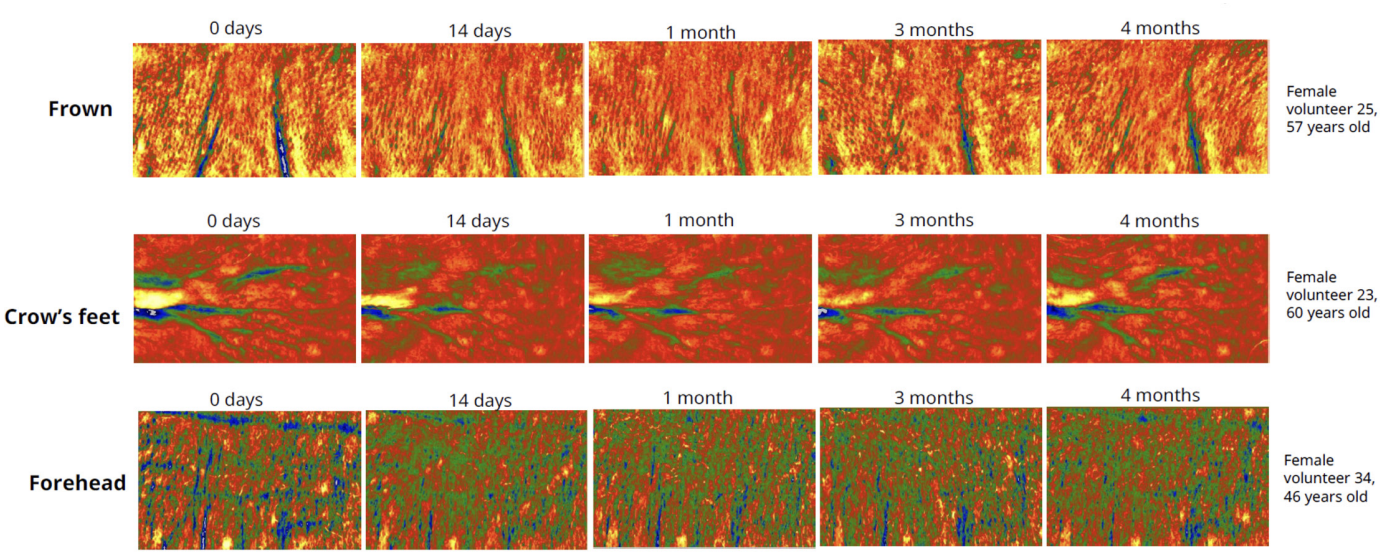

Male volunteer 26, 47 years old

Visibility of wrinkles with a relaxed expression

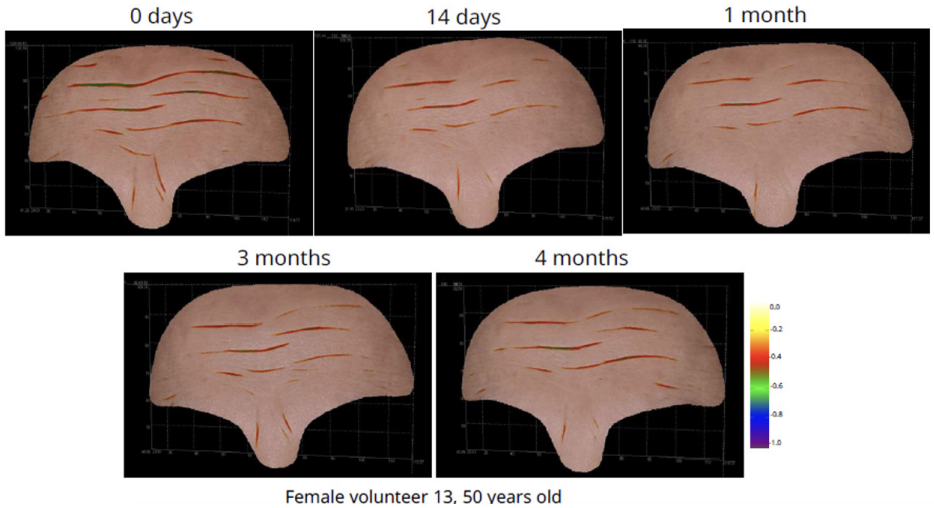
Skin roughness (Ra) vs 14 days

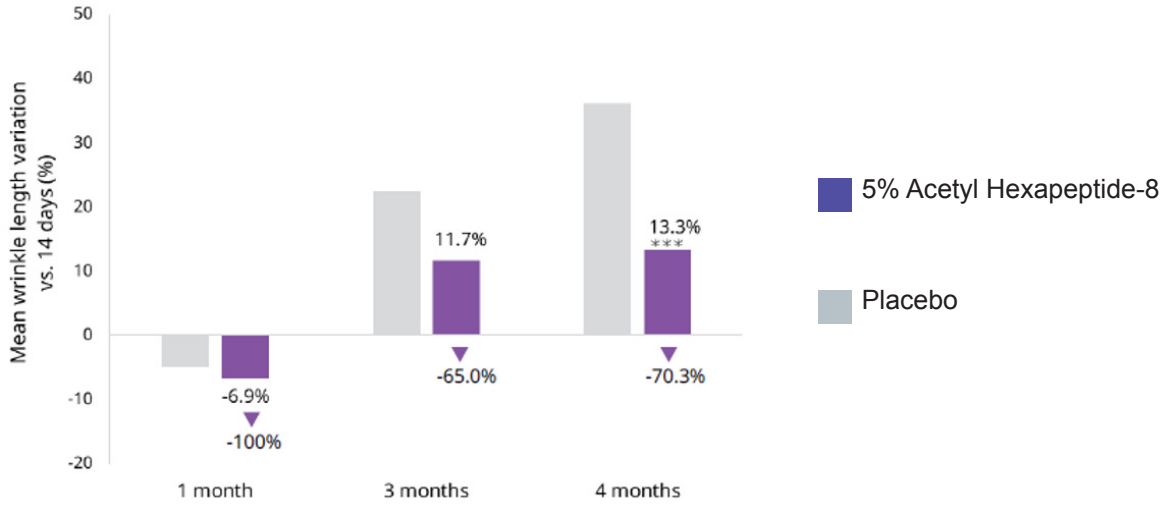



Acetyl Hexapeptide-8 helps prolong the effect of botulinum toxin injections, resutling in smoother skin for longer.




Wrinkle length on forehead and frown vs 14 days






Boosting the efficacy of botulinum toxin injections by minimising the visibility of the most prominent wrinkles.

Links:
https://pubmed.ncbi.nlm.nih.gov/24754410/
https://pubmed.ncbi.nlm.nih.gov/23417317/
https://www.ncbi.nlm.nih.gov/m/pubmed/29371611/?i=1&from=Argireline
Data on file