

SYN[®]-HYCAN

*Hyaluronic Acid booster:
firming and remodeling from within*

CB



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Peptides | Pharma-inspired skincare

Restored
skin
volumes

dsm-firmenich 

Restoring Lost Volume

A New Focus in Beauty Care

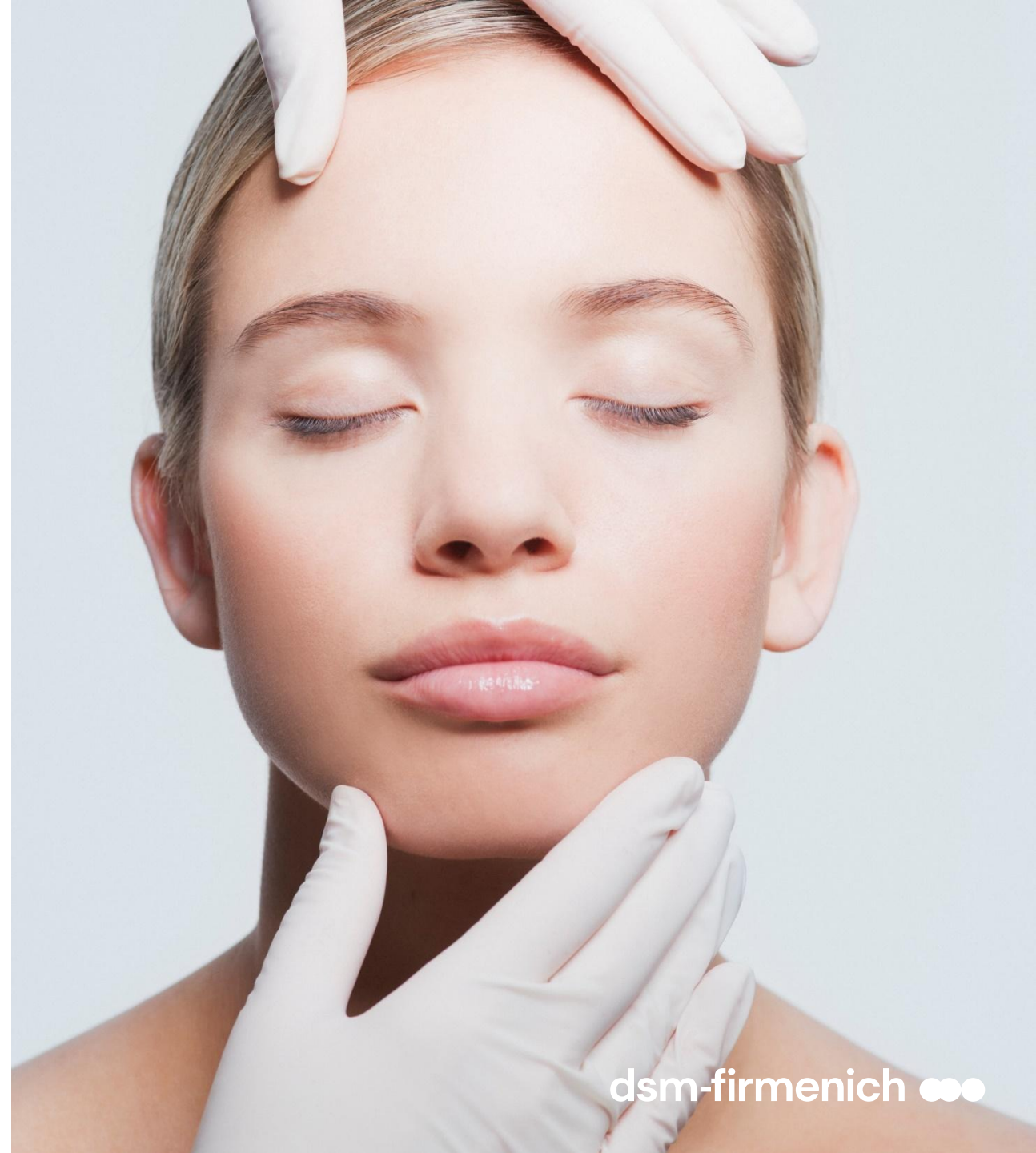
In cosmetic dermatology, wrinkles and sagging skin are no longer viewed in isolation.

The new focus includes how loss of volume in one area of the face impacts the appearance of other areas.

Over time, facial skin loses volume in key areas, including the cheeks, under eyes, the jawline and around the mouth.

Fillers counteract this process by adding fullness to needed areas, restoring skin to its original position.

The New York Times, "The Filler Effect", Huffington Post, "What is a Non-Surgical Face Lift?"



Hyaluronic Acid: The Rising Queen of Fillers

Their reversible and natural-looking effects make HA fillers highly desirable

Different facial zones that can be augmented by dermal fillers

- Creases between eyebrows
- Droopy eyebrows
- Hollow temples
- Loss of volume in cheeks
- Ear lobe correction
- Hollowness under eyes
- Laugh lines
- Thin lips
- Chin wrinkles
- Marionette lines
- Undefined jawline
- Sagging corners of mouth
- Lipstick lines
- Undefined nose or tip

5.5 millions

Hyaluronic acid procedures performed in globally in 2023

40%

share of dermal filler procedures using hyaluronic acid

#2 non-invasive procedure

hyaluronic acid were second most frequently performed procedure

after Botox®

Fastest growing procedure

+29,1% vs. 2022

HA procedure growth outpaced Botox®, chemical peels, laser hair removal, and microdermabrasion²

Source: International Society of Aesthetic Plastic Surgery International Survey 2023

Hyaluronic Acid still on hype

New methods and consumer interest also remains strong

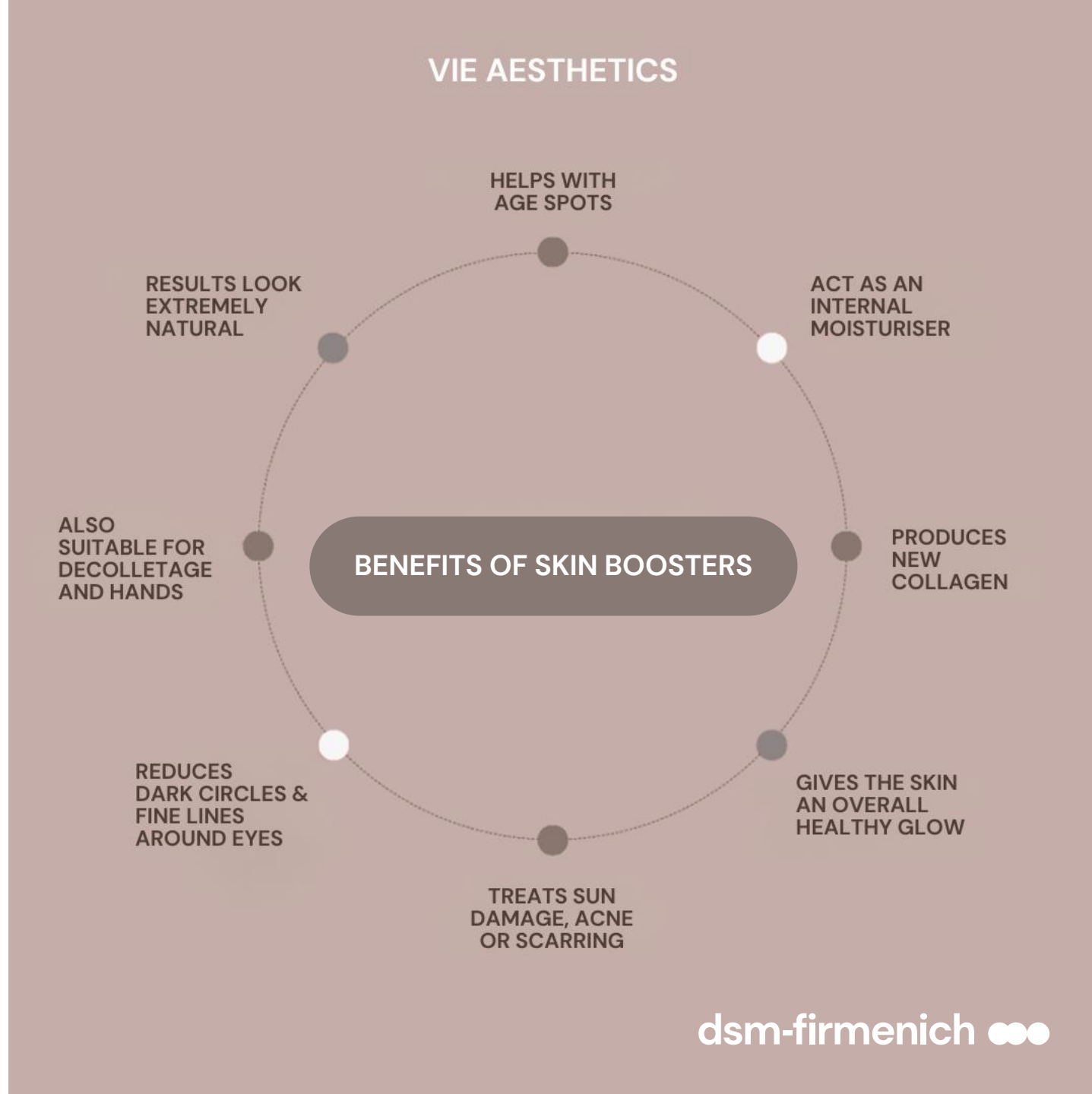
Latest trend: Skin Boosters

New method of hyaluronic acid. It involves the application of HA's microinjections aiming boosting hydration, glow and collagen production, following recent consumer needs for more healthier and natural-look skin for longer.

It has HA as the primary substance and can also combine other actives.



[What are skin boosters & do they work? | Our Blog | Eason Aesthetics \(dermalfillersbromley.co.uk\)](#)
[Skin Booster Injectables Explained: What Is Skinvive, Profhilo? Experts Weigh In \(harpersbazaar.com\)](#)
[Skin Boosters: Why the Hype? - Vie Aesthetics \(vie-aesthetics.com\)](#)



HA-Inspired Cosmetics Continue to Rise

New Hyaluronic Acid products continue to evolve and sophisticating



LA ROCHE-POSAY
Hyalu B5 Booster 5x

Immediate lifting and boosts.
Intensively repairs skin in 1h.
Anti-wrinkles results in 1 week.
Tested as post-procedure



SKINCEUTICALS
H.A. Intensifier Multi-Glycan

Instantly plumps skin and also boosts
skin glycans for even higher
volumizing results.



VICHY LABORATORIES
LIFTACTIV H.A. EPIDERMIC FILLER

Claims to recharg 100% of Hyaluronic
Acid Epidermal Daily loss, providing
intense volumizing benefits on skin.



SKINMEDICA
LIFTACTIV H.A. EPIDERMIC FILLER

Developed by the creators
of BOTOX® , this serum uses a
proprietary complex of hyaluronic
acid providing deeper hydration for
visible plumpness and radiance.

Sources: ¹ [Lancome-USA.com](https://www.lancome-usa.com) ² Mintel GNPD 2018 ³ [Barneys.com](https://www.barneys.com) ⁴ [Skinceuticals.com](https://www.skinceuticals.com)

Hyaluronic Acid in skin

Skin contains the majority of the body's HA

Key Facts About Hyaluronic Acid

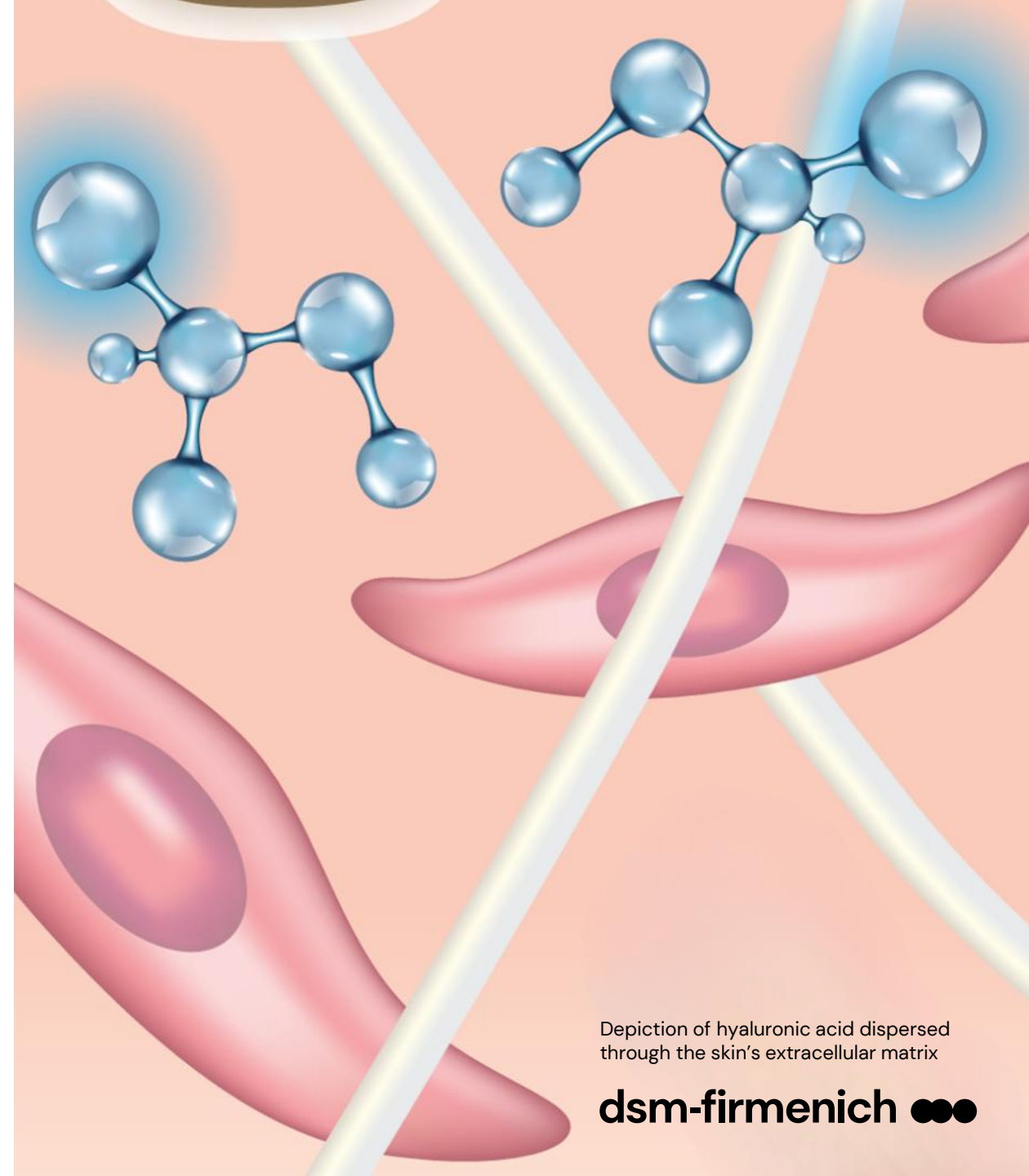
Hyaluronic Acid belongs to the Extracellular Matrix (ECM) molecules and is the most predominant component of the ECM.

In humans, HA is the most abundant in skin, accounting for 50% of the body's HA.

Hyaluronic acid is co-located with CD44, a prominent HA cell receptor, which is found on virtually all cells and acts as an HA anchor.

Functions of HA:

- Hydration
- A space filling capacity
- Framework through which cells migrate



Depiction of hyaluronic acid dispersed through the skin's extracellular matrix

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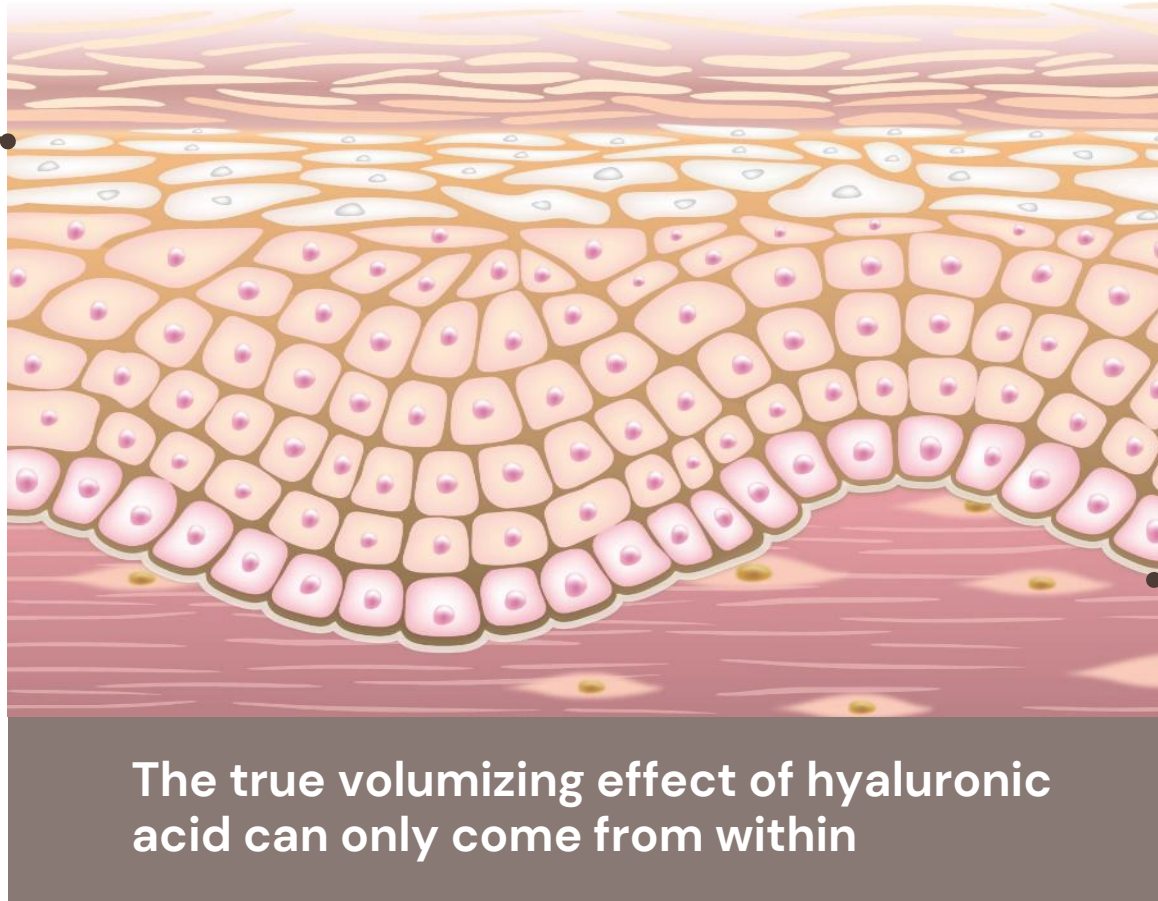
The Purpose of Hyaluronic Acid in Skin

Hydration and Skin Structuring are the main roles of HA

Skin Moisture: Epidermal HA

Impact of Lost Epidermal HA

With age, there is a marked decrease of epidermal HA, the principal molecule responsible for binding and retaining water molecules, resulting in loss of skin moisture



Skin Volume: Dermal HA

Impact of Lost Dermal HA

Dermal HA serves as a framework for structural proteins (e.g. collagen, elastin) and skin cells. Loss of dermal HA leads to less volume and mechanical cushioning and loss of skin moisture.

SYN®-HYCAN CB

Hyaluronic acid booster: firming
and remodelling from within

Boosts skin's own production of hyaluronic
acid, with proven benefits on multiple skin
zones, leading to fuller, firmer skin in weeks



SYN®-HYCAN CB

ID Card

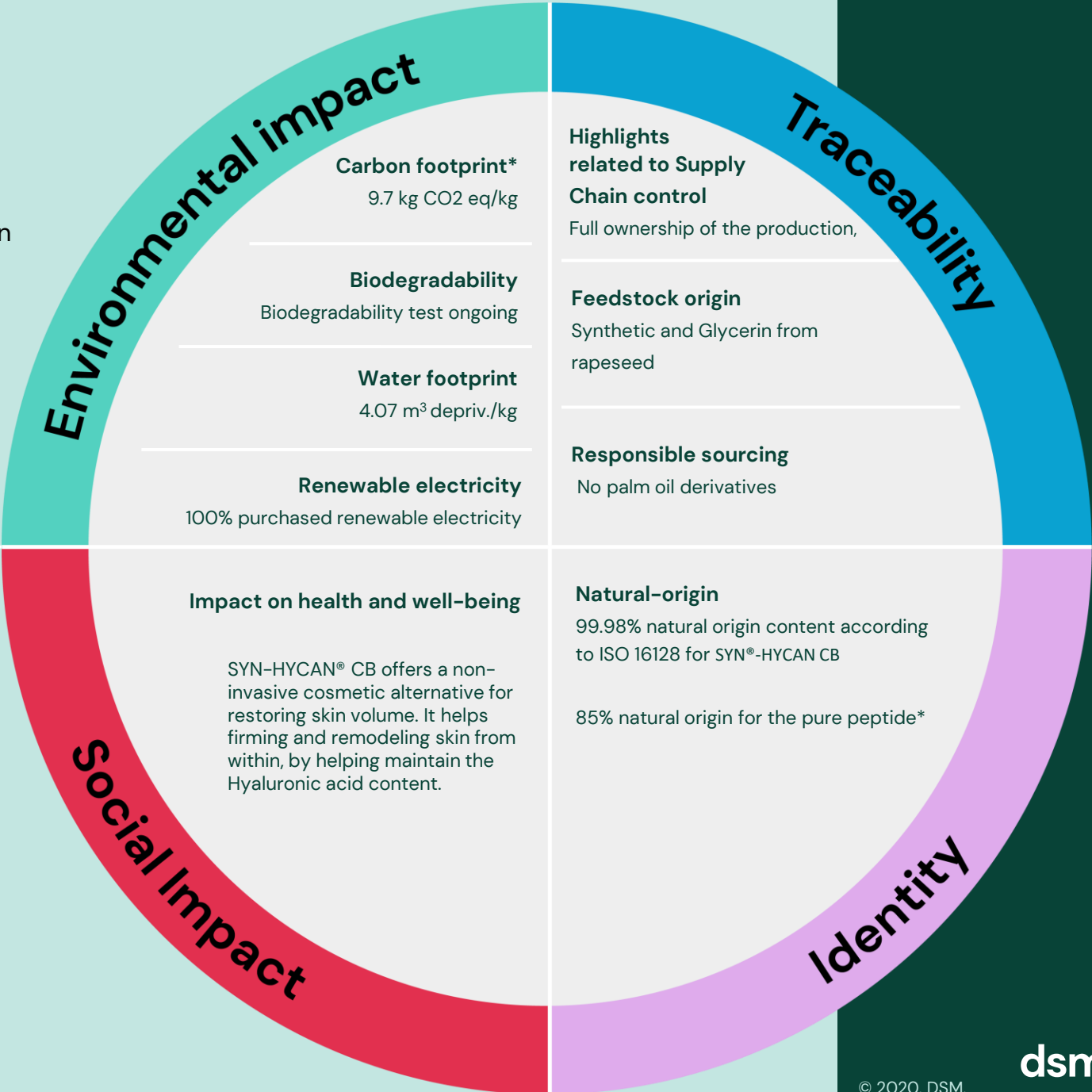
INCI NAME:		Tetradecyl Aminobutyroylvalylaminobutyric Urea Acetate, Glycerin, Aqua, Magnesium Chloride			
TECHNOLOGY:	Highly potent, natural origin tripeptide, suitable for Clean-Beauty, produced via Green Chemistry Science with an optimized SYN®-Peptide technology, designed to stimulate hyaluronic acid from within		- Original SYN®-HYCAN peptide generation patented; CB version patent application pending - TFA-free¹ 99.98% natural origin (ISO 16128) for SYN®-HYCAN CB – 85% natural origin (ISO 16128) for the pure SYN®-HYCAN peptide²		
TECHNICAL:	Form: Liquid	Use level: 2-5%	Solubility: Miscible in water		
	pH of use: 3.0-5.5	Preservative: Free			
BENEFITS:	- Boosts hyaluronic acid (HA) synthesis in both keratinocytes and dermal fibroblasts* - Increases CD44 expression, a key cellular anchor of HA* - Increases collagen type 1, lumican and decorin levels, important for collagen support & organization*		- Provides visible filling effect in just 2 weeks - Lifts even the most difficult areas, such as the neck - Benefits on multiple skin zones (under eye, upper- and mid-cheek, jawline, neck, lip) - Increases skin firmness +200% on cheek area.		
REGISTRATION CERTIFICATION:		NATURAL ORIGIN 99.98% ISO 16128 SYN®-HYCAN CB NATURAL ORIGIN 85% ISO 16128 SYN®-HYCAN CB PEPTIDE VEGAN FRIENDLY VEGAN VEGAN HALAL HALAL CERTIFIED ISLAMIC FOOD COUNCIL OF EUROPE HALAL			

SYN®-HYCAN CB

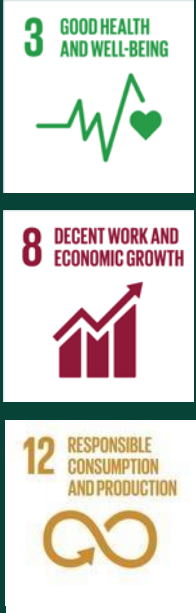
INCI name: Tetradecyl
Aminobutyroylvalylaminobutyric Urea
Acetate, Magnesium Chloride, Aqua, Glycerin
Product Code: 5017794

PIONEER IN PEPTIDES
High performance active with low carbon footprint contribution.

Natural origin peptide suitable for Clean-Beauty, produced via Green Chemistry with an optimized synthesis



Aligned with and contributing to the
SUSTAINABLE DEVELOPMENT GOALS



The carbon and water footprint calculations are based on internally conducted LCA according to ISO 14040/44 guidelines, dsm-firmenich LCA policy and validated by internal reviewers.

The natural origin Index is at 0.85 according to the ISO 16128 standard

Peptides | Pharma-inspired skincare

SYN®-HYCAN CB

A natural peptide for sustainable formulations



Carbon footprint of 9.7 kg CO₂ eq./kg. High efficiency allowing a low carbon footprint in use¹



SYN-HYCAN® CB suitable for Clean-Beauty with TFA free process². Natural-origin peptide (0.85 natural origin Index according to ISO 16128).



Green chemistry reaction type³ with an optimized synthesis reducing the number of steps (8 vs 14 steps previously).



Switch from a solid phase to a liquid phase process, allowing for significantly reducing amounts of solvents and for including greener solvents.



Production with **no CMR solvents** and no CMR reagents

1. Considering a 1-3% concentration of SYN-HYCAN® CB in final formulation, 97-291g CO₂ per kg in final formulation.
2. TFA replaced with acetic acid.
3. Main reaction type is amidation



dsm-firmenich peptides technology

core principles

- Mimicking body's own key biological pathways with synthetic peptides
- Target specific modification of existing structures to improve selectivity and activity

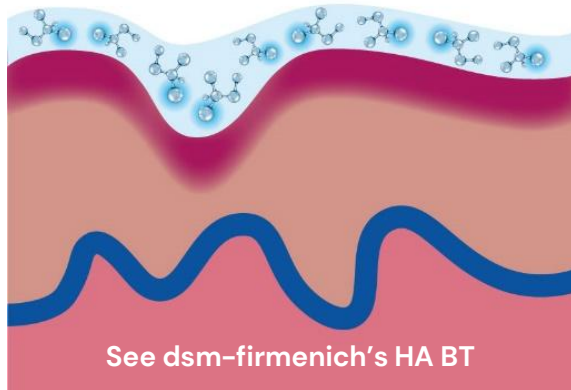
Key success factors

- Small peptide size (tri-, tetra peptides) for best efficacy
- Fully substantiated, visible results on the skin
- Chemically well-defined structure
- Extended safety dossier
- High purity and stability
- No preservative



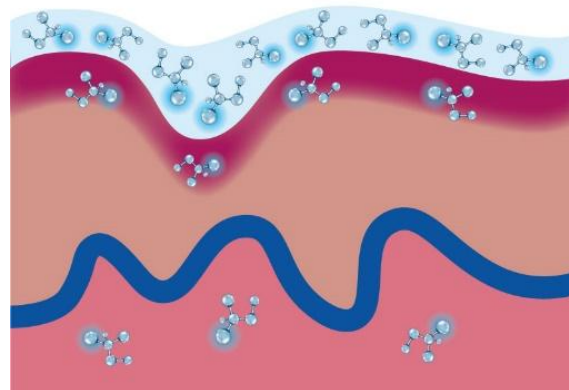
SYN®-HYCAN CB

The advantage of building from within



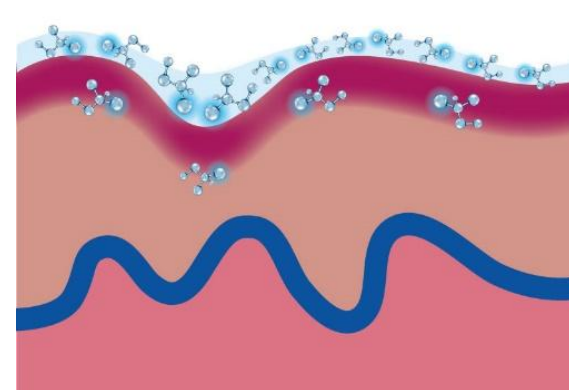
Topical long chain HA

- Excellent humectant
- Very limited effect on skin's intrinsic HA
- Natural chain length similar to skin (2-3 mda)



ultra-short chain HA

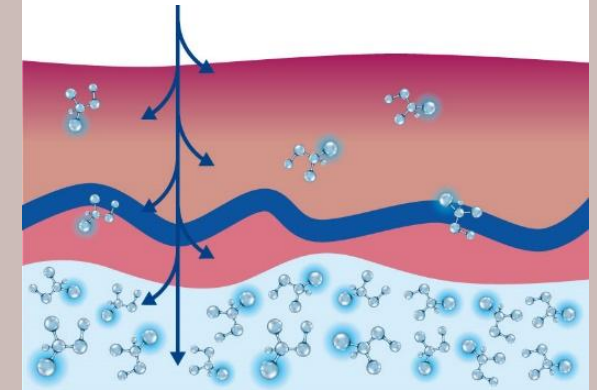
- Good humectant
- Limited effect on skin's intrinsic HA, with limited penetration
- Much smaller than body own HA



Topical short chain HA

- Good humectant
- Limited effect on skin's intrinsic HA
- No similarity in length with skin's HA (50kda)

SYN®-HYCAN CB

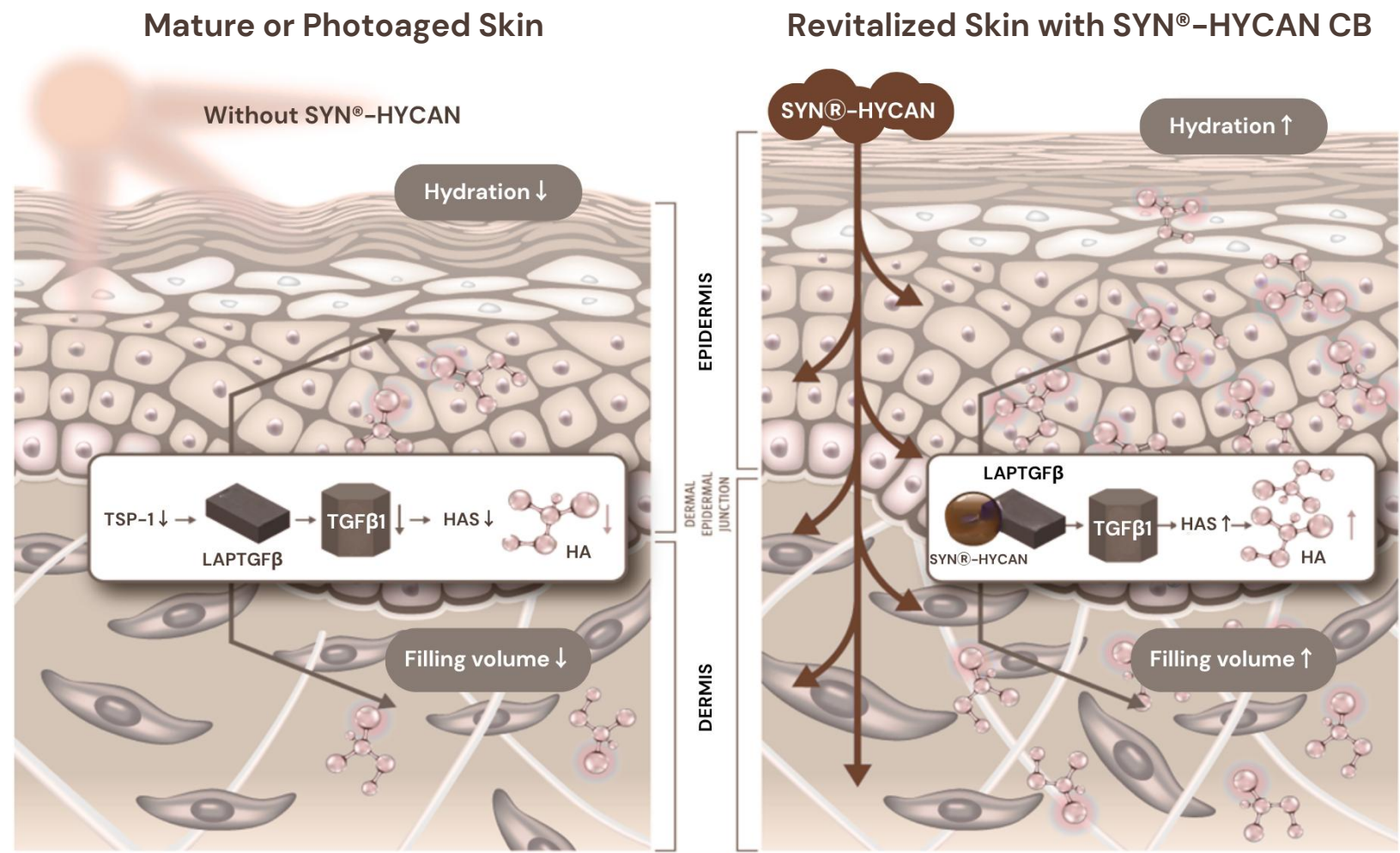


SYN®-HYCAN CB

- Excellent hydrating effect plus skin firming
- Boost skin's own HA production
- Natural HA composition and location

SYN®-HYCAN CB Mimicking TGF-Beta activation for Increased HA Synthesis

- Low Thrombospondin
- Low TGFβ1 activation
- Less hyaluronic acid
- Less volume
- Dry skin



SYN®-HYCAN CB mimics Thrombospondin
TGFβ1 activation
More hyaluronic acid
More volume
Hydrated skin

SYN®-HYCAN CB – *in vitro* efficacy

Study details

Hyaluronic Acid Synthesis

- Epidermal Keratinocytes, dose response
- Dermal Fibroblasts, versus benchmark peptide
- Skin explants analysis, *ex vivo*

Hyaluronic Acid Cellular Anchoring

- 3D Microsphere HA analysis, visual assessment
- CD44 Hyaluronic Acid Receptor expression assay

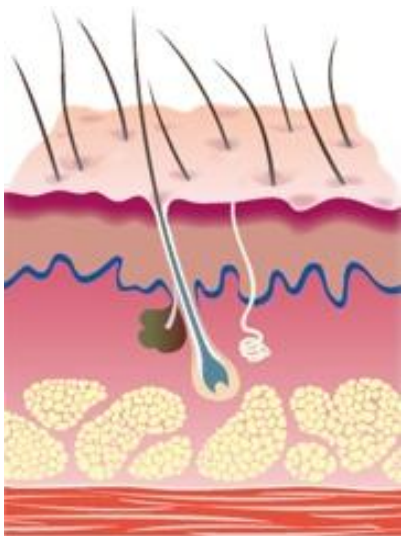
Collagen Support & Organization

- Proteoglycan synthesis
- Collagen synthesis

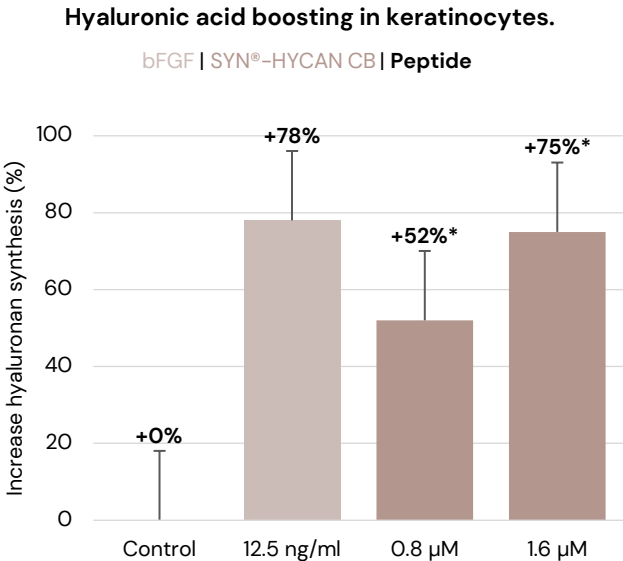
in vitro

HA Synthesis boost in Keratinocyte & Fibroblast Cell Culture

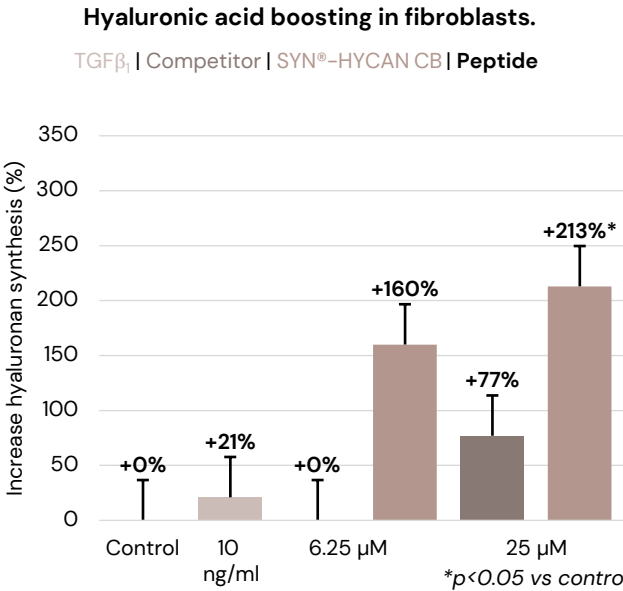
in vitro



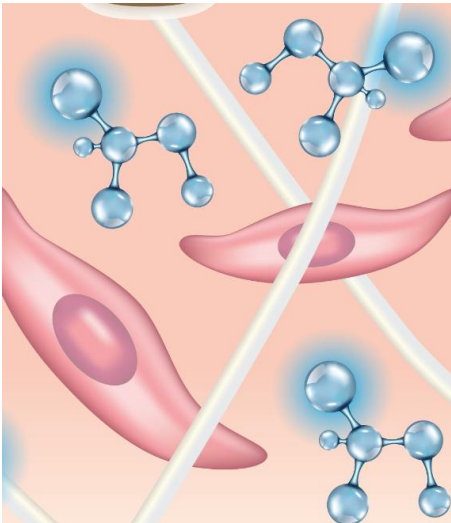
Normal human keratinocytes were incubated without FCS for 3 days.



SYN®-HYCAN CB peptide provides moisturizing from within by HA synthesis in the epidermis.



SYN®-HYCAN CB peptide increases hyaluronic acid synthesis by a factor of 3!



Normal human fibroblasts (NHF) were incubated without FCS for 3 days.

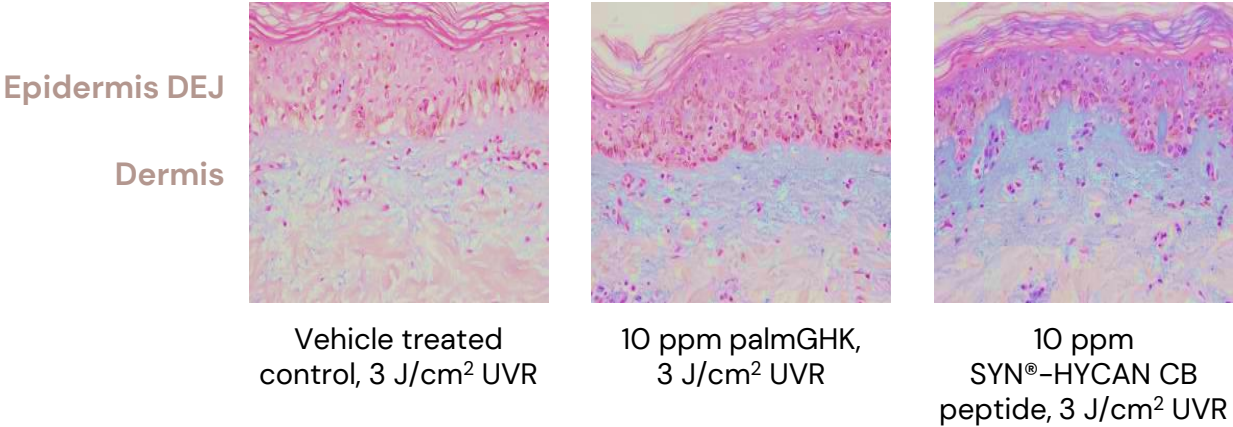
SYN®-HYCAN CB peptide can boost hyaluronic acid synthesis in both keratinocytes and dermal fibroblasts **3x better than a competitor peptide after three days treatment.**



The Advantage of Building from Within

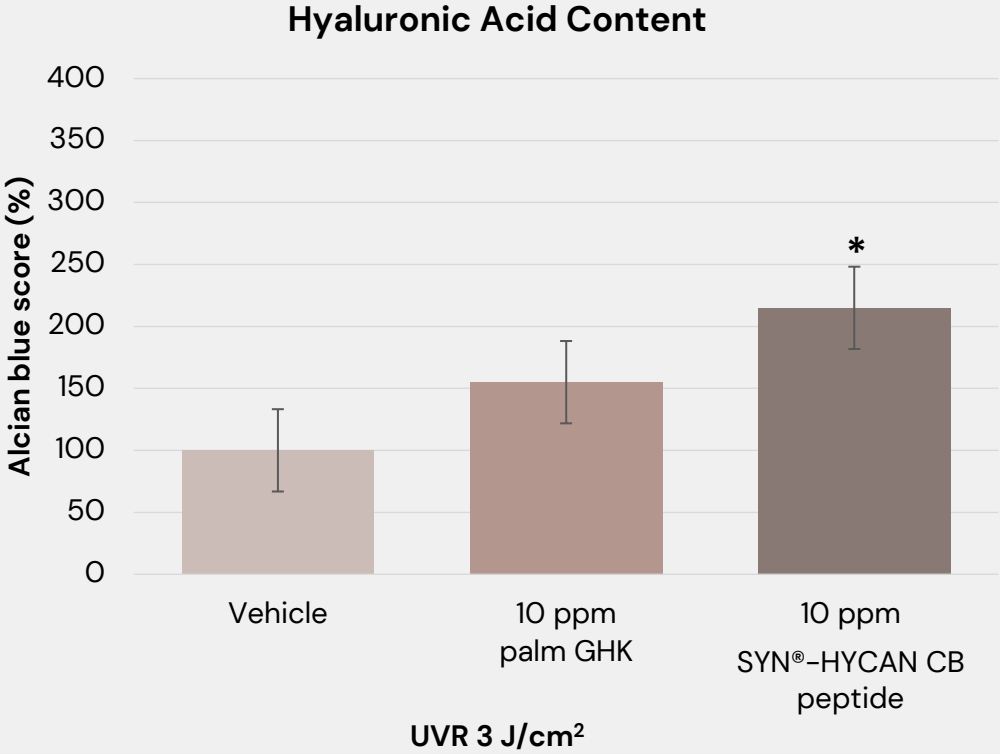
ex vivo

SYN®-HYCAN CB peptide boosts hyaluronic acid synthesis in skin ex-vivo by 3x



↙

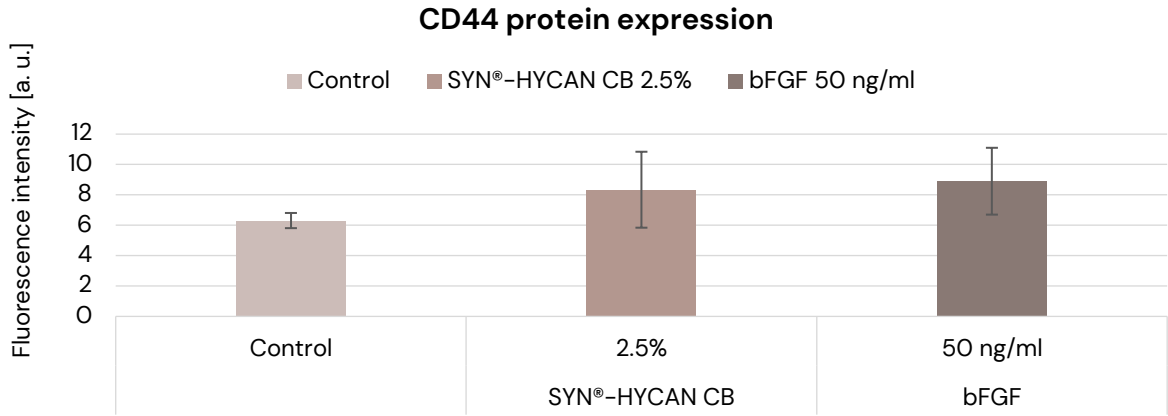
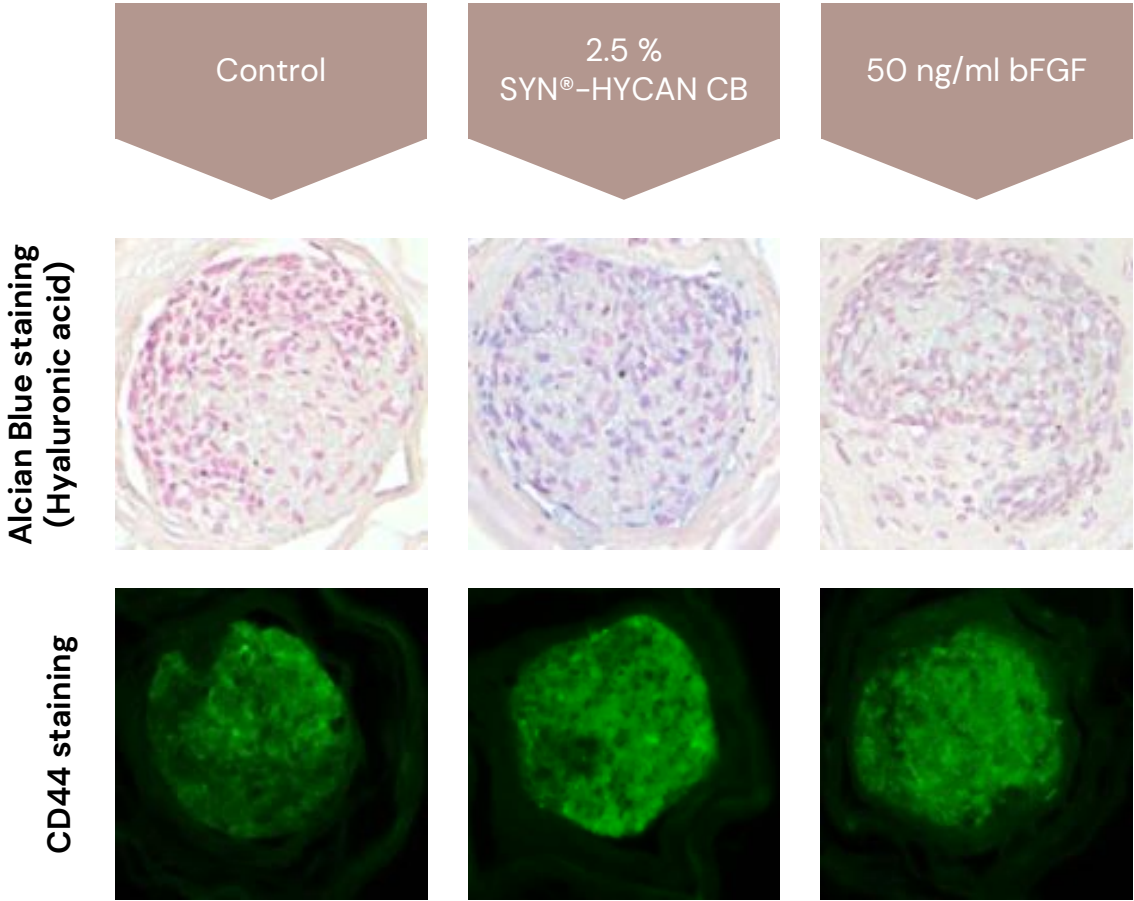
Hyaluronic acid synthesis (blue staining) is significantly increased in human skin explants treated with UV-radiation after six days topical incubation with the SYN®-HYCAN CB peptide.



Hyaluronic Acid Cellular Anchoring

CD44 (HA Receptor) Expression Assay

in vitro



SYN®-HYCAN CB enhances CD44 expression, a key cellular anchor of HA, in skin microspheres



CD44 is the most prominent hyaluronic acid (HA) receptor in skin and found on virtually all cells. In the dermis and epidermis, HA is co-localized with CD44.

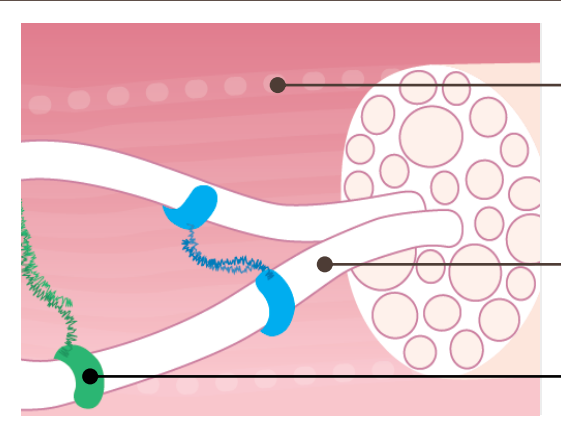


Skin microspheres, a novel cutaneous model with a dermal core and an epidermal outer layer, was incubated with 2.5% SYN®-HYCAN CB or a control growth factor (bFGF) for 10 days. HA was visualized by alcian blue (blue staining), and CD44 was measured by antibody staining (green fluorescence).

Midgley et al. 2013 JBC 288 (21):14824 –14838
 Simpson et al. 2010 AJP 176 (3):1215 – 1228

Collagen Organization

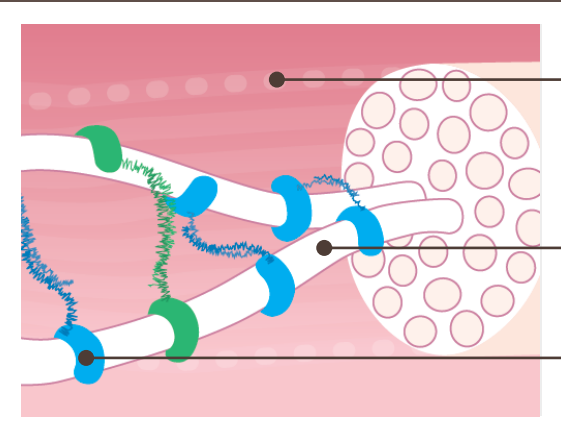
Proteoglycan Synthesis



Lower decorin and lumican levels in aging skin

Irregular collagen fibril structure

Weak fibers



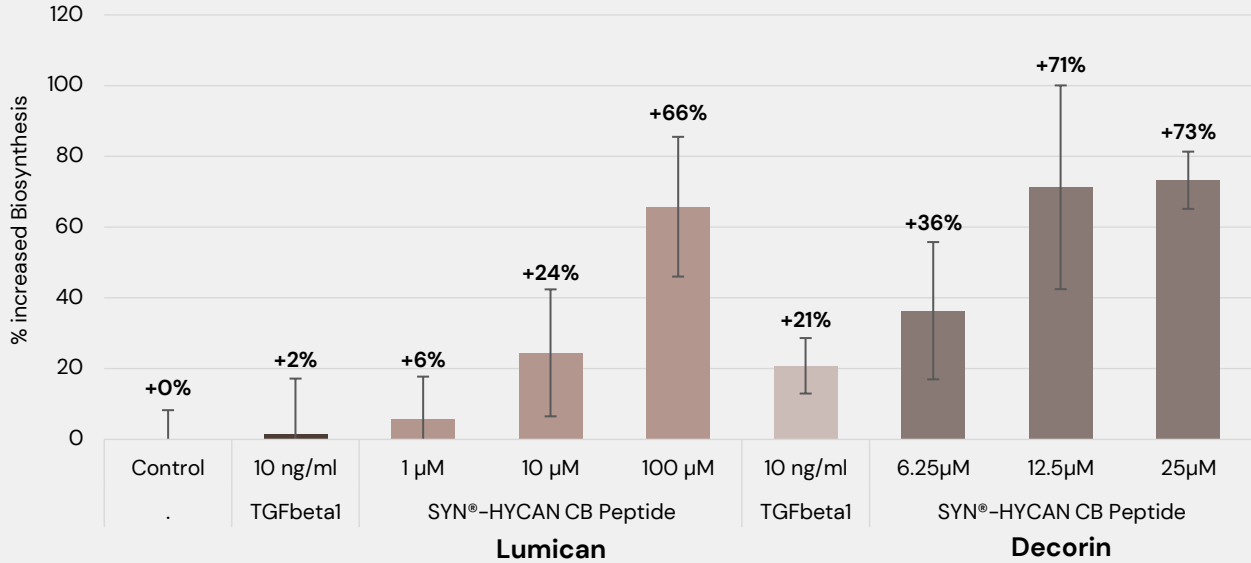
Healthy skin with increased decorin and lumican levels

Smaller width of collagen fibrils

Strong fibers

in vitro

Normal human fibroblasts (NHF) were incubated without FCS for 3 days.
Detection: enzyme linked immunoassay (EIA)



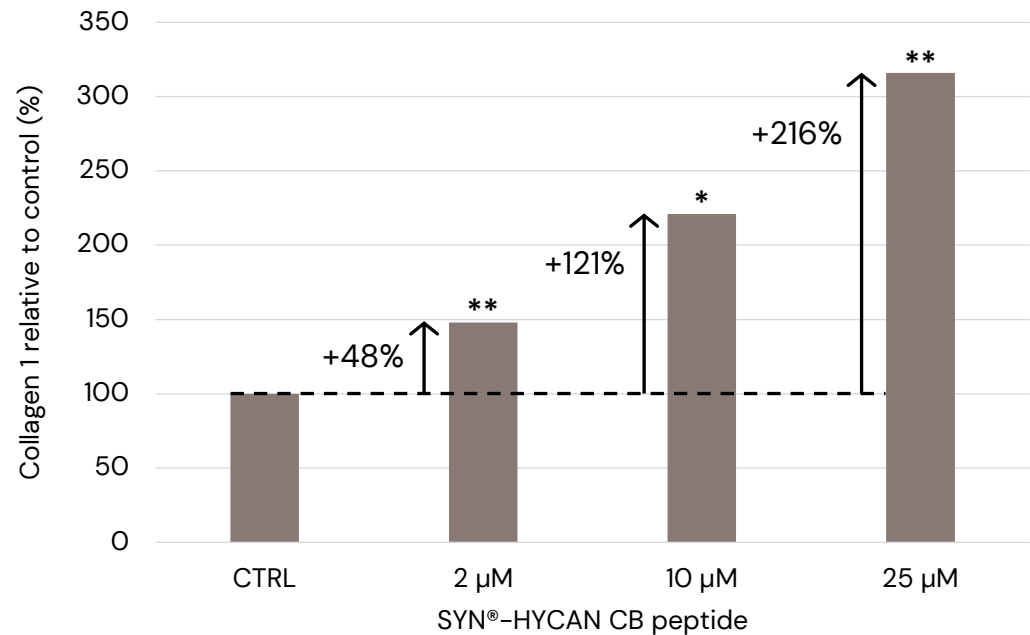
SYN®-HYCAN CB peptide increases lumican and decorin levels

Collagen Support

Collagen 1 Synthesis

in vitro efficacy

Test performed on human dermal fibroblasts



For the SYN®-HYCAN CB peptide, the following applies:

2 μM	=	0.00012%	=	1.2 ppm
10 μM	=	0.0006%	=	6 ppm
25 μM	=	0.0015%	=	15 ppm

SYN®-HYCAN CB peptide increases Collagen 1 levels

* p< 0.05 compared to untreated cells (ctrl).
** p<0.005 compared to untreated cells (ctrl)

SYN®-HYCAN CB – *in vivo* efficacy

Study details

Skin Firmness and Remodeling

- AEVA-HE 3D facial volume analysis
- DynaSKIN firmness analysis
- PRIMOS Body neck and double chin contour analysis

Skin Hydration

- Corneometer analysis

Consumer-Perceivable Benefits

- Volunteer Self-Assessment

in vivo



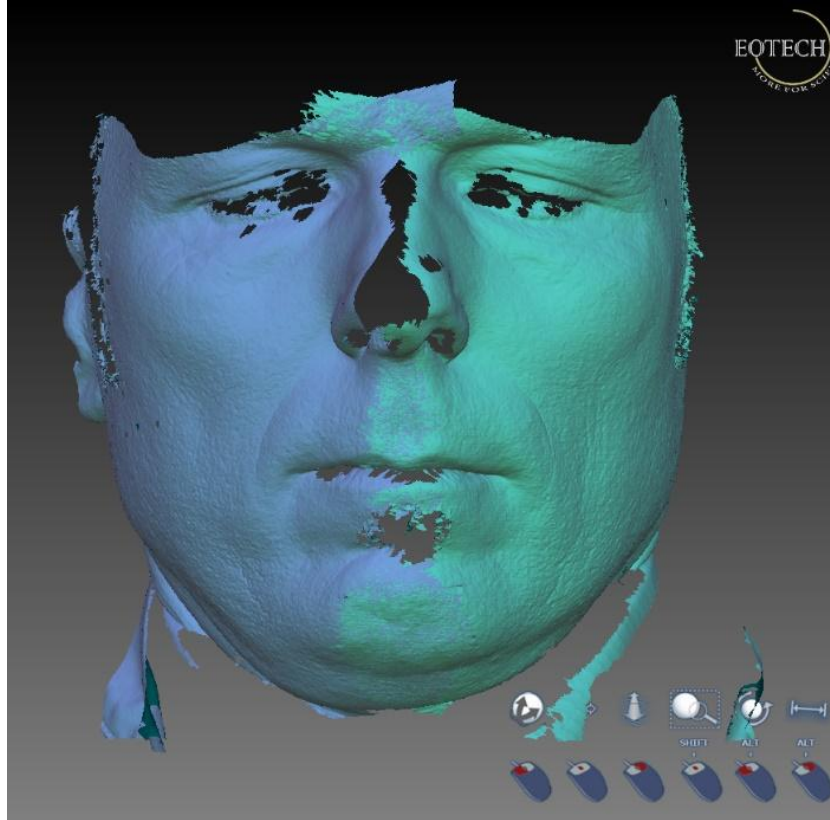
Skin Firming and Remodeling

Positive Volume Assessment, AEVA-HE, Eotech, France

in vivo

High resolution 3D image capture software which measures skin topography, face topology and body morphology changes. From the capture of the three-dimensional structure, the parameter positive volume was measured at various points of the face.

A positive volume indicates a filling effect, where the facial area is fuller at the final test point versus the beginning of the study.



Skin Firming and Remodeling

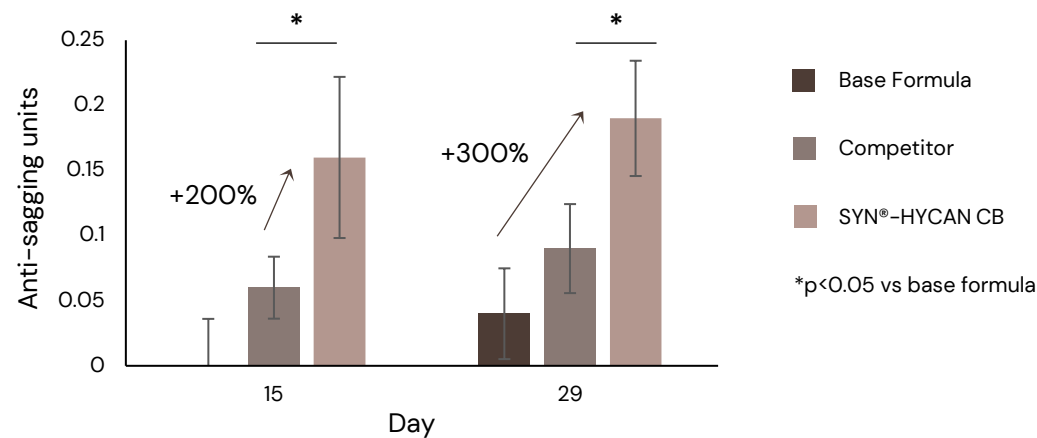
Positive Volume Assessment, AEVA-HE, Eotech, France

in vivo

Instrumental Evaluation

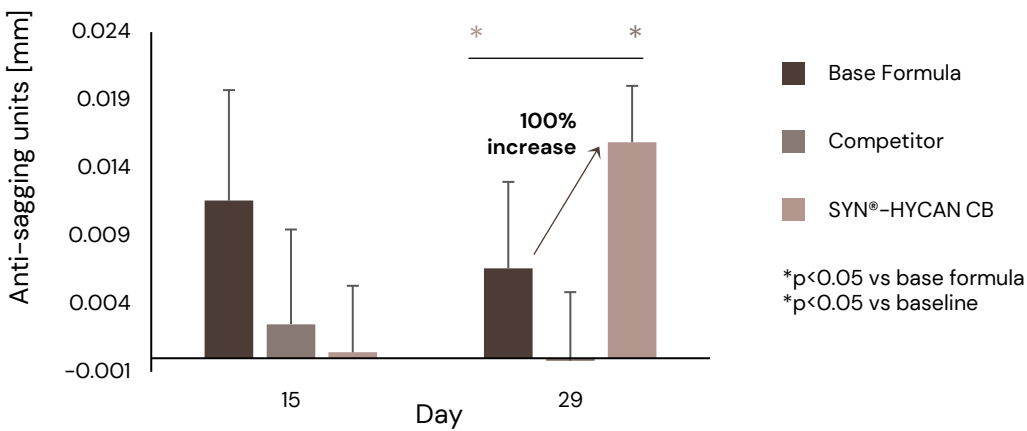
Twice daily application for 1 month of a formulation with or without 2.5% SYN®-HYCAN CB or 3% of a competitor on full face. Caucasian female volunteers (30 per group) were between ages 40–60 with visible skin sagging on the face. Double-blind, placebo-controlled, randomized. Groups run in parallel. Measurement of skin distance change done on multiple facial sites.

Skin filling assessment, area below eyes (Zone 1)



Positive Volume	SYN®-HYCAN CB	
	T 15 Days	T 29 Days
Positive Responders	72%	78%

Skin filling assessment, jawline (Zone 4)



Positive Volume	SYN®-HYCAN CB	
	T 15 Days	T 29 Days
Positive Responders	n/a	76%

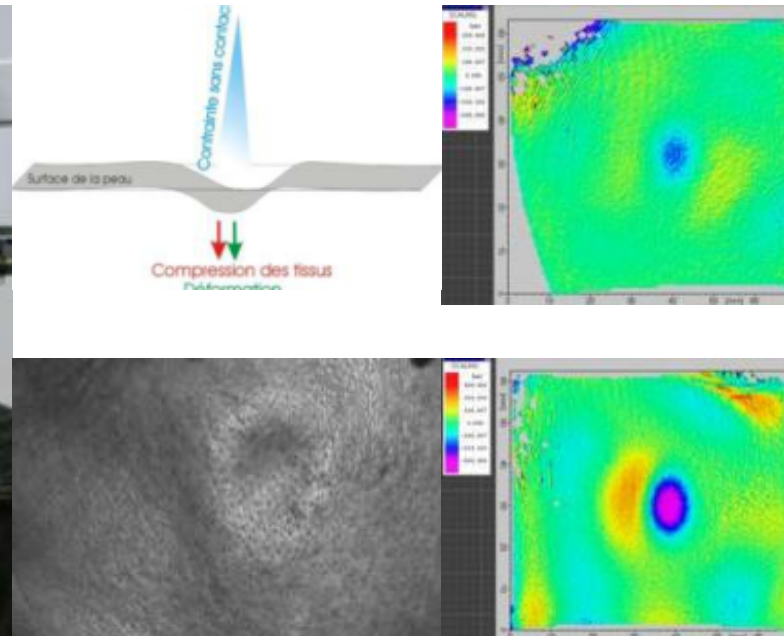
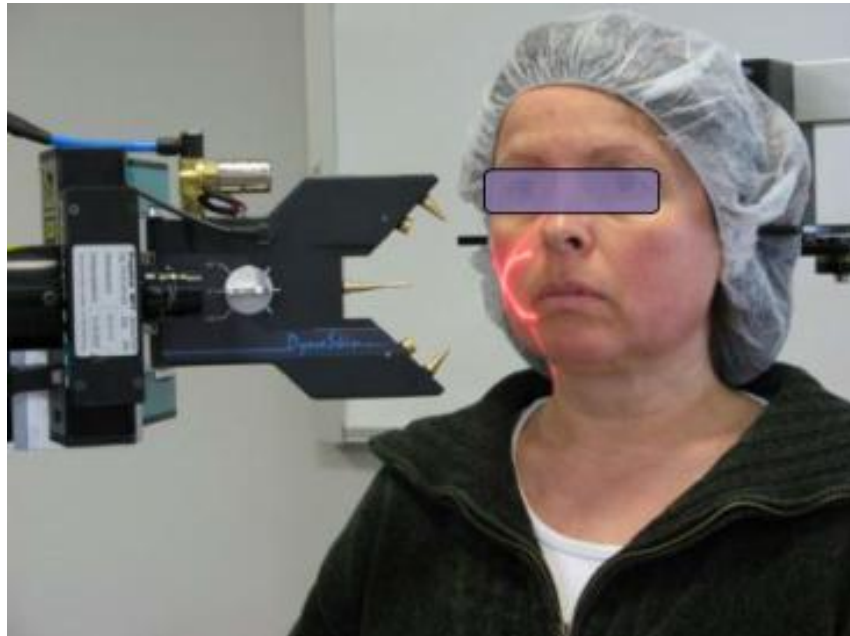
SYN®-HYCAN CB provides visible filling effect up to 3x better than competitor in just 2 weeks.

Skin Firming and Remodeling

Firmness Assessment, DynaSKIN

in vivo

A complete non-contact method to assess skin firmness before and after treatments under very reproducible conditions. The device utilizes air pressure to create a deformational in the skin area of interest, with an air stream perpendicular to the skin surface. T parameter **volume** was measured on the cheek area. **A decrease in volume indicates a firming effect here**, as skin is more resistant to deformation.



Young Volunteer

- High degree of firmness
- Very little deformation
- High resistance to stress

Elder Volunteer

- Low degree of firmness
- Significant deformation
- Low resistance to stress

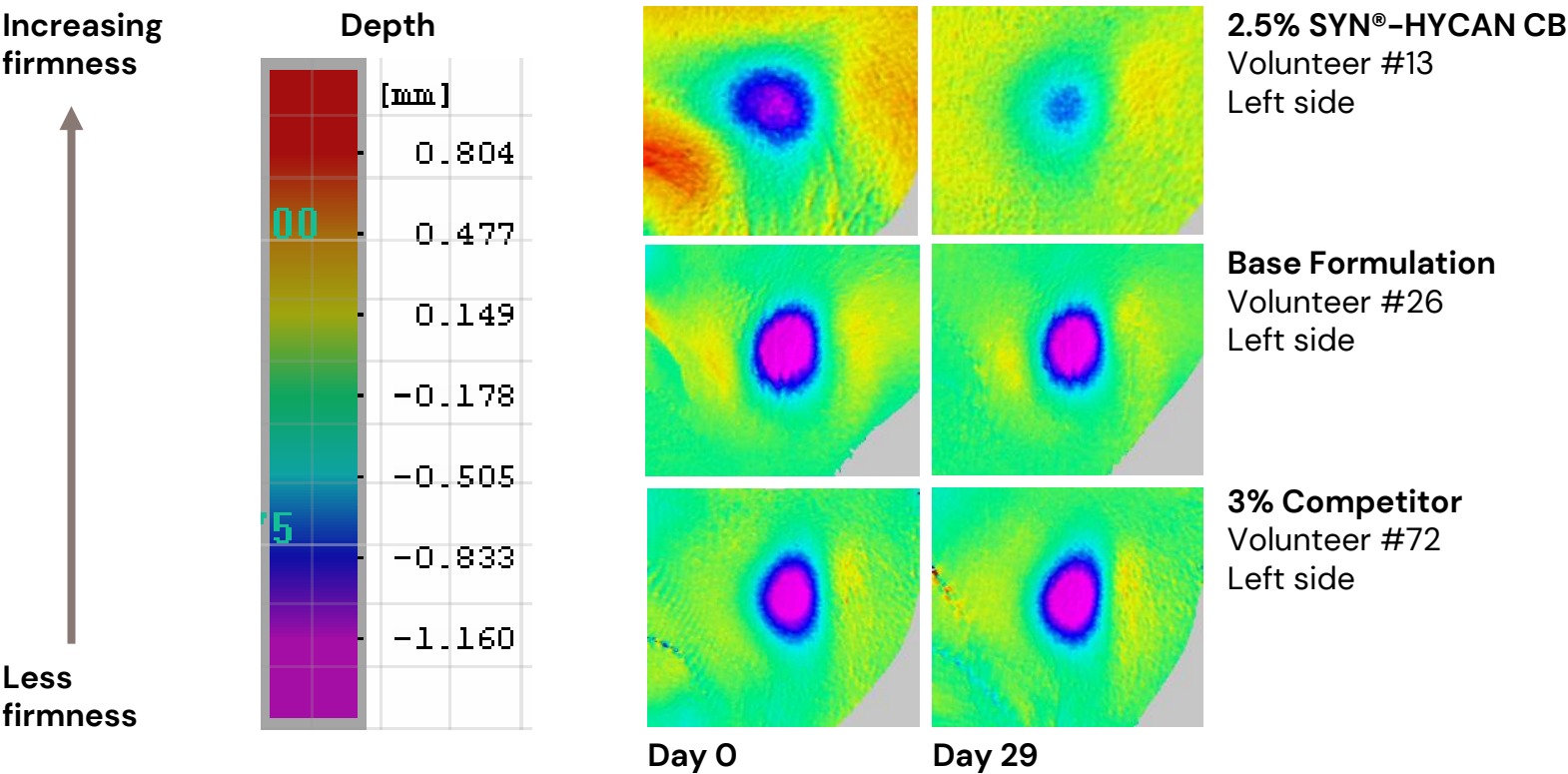
Skin Firming and Remodelling

Firmness Assessment, DynaSKIN

in vivo

Instrumental Evaluation

Twice daily application for 1 month of a formulation with or without **2.5% SYN®-HYCAN CB** or 3% of a competitor on full face. Caucasian female volunteers (30 per group) were between ages 40–60 with visible skin sagging on the face. Double-blind, placebo-controlled, randomized. Groups run in parallel. Measurement of firming effect performed on the cheek area.



SYN®-HYCAN CB restores firmness for mature skin

Skin Firming and Remodelling

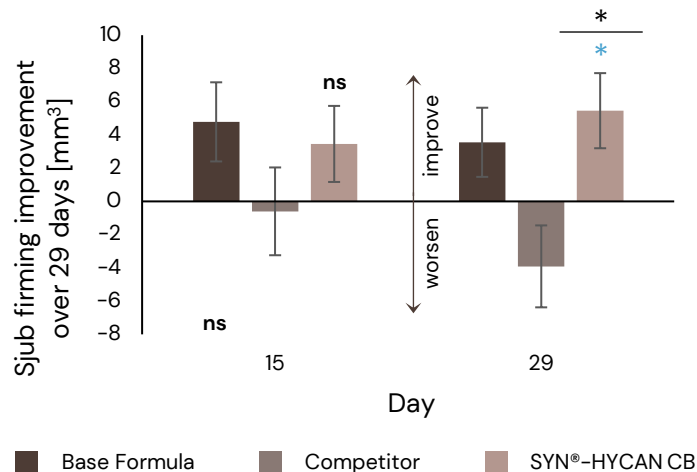
Firmness Assessment, DynaSKIN

in vivo

Instrumental Evaluation

Twice daily application for 1 month of a formulation with or **without 2.5% SYN®-HYCAN CB** or 3% of a competitor on full face. Caucasian female volunteers (30 per group) were between ages 40–60 with visible skin sagging on the face. Double-blind, placebo-controlled, randomized. Groups run in parallel. Measurement of firming effect performed on the cheek area.

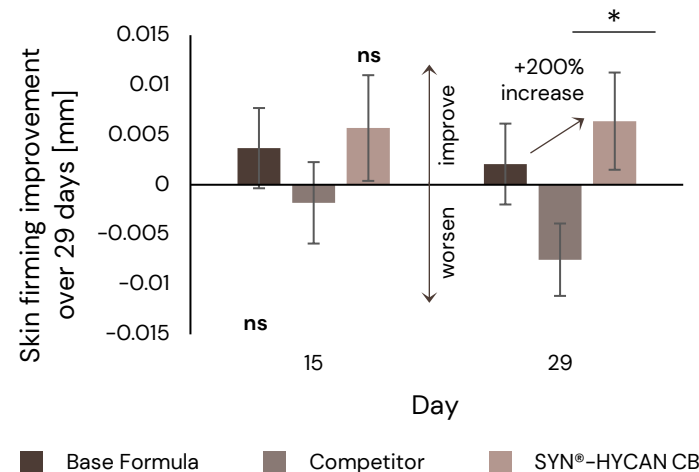
Volume, cheek area (Zone 3)



Volume (Firmness) Improvement:

- -9.6% p<0.05 vs baseline, up to -53%
- Responders 72%

Depth, cheek area (Zone 3)

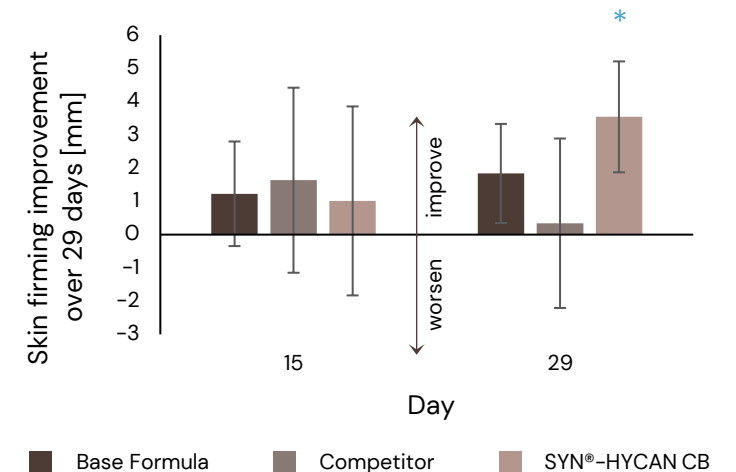


Depth Improvement:

- -4.1% vs baseline, up to -37%
- Responders 62%

*p<0.05 vs competitor
*p<0.05 vs baseline

Circumference, cheek area (Zone 3)



Circumference Improvement:

- -3.5% p<0.05 vs baseline, up to -22%
- Responders 72%

Only SYN®-HYCAN CB significantly increases skin firmness +200%

Skin Hydration

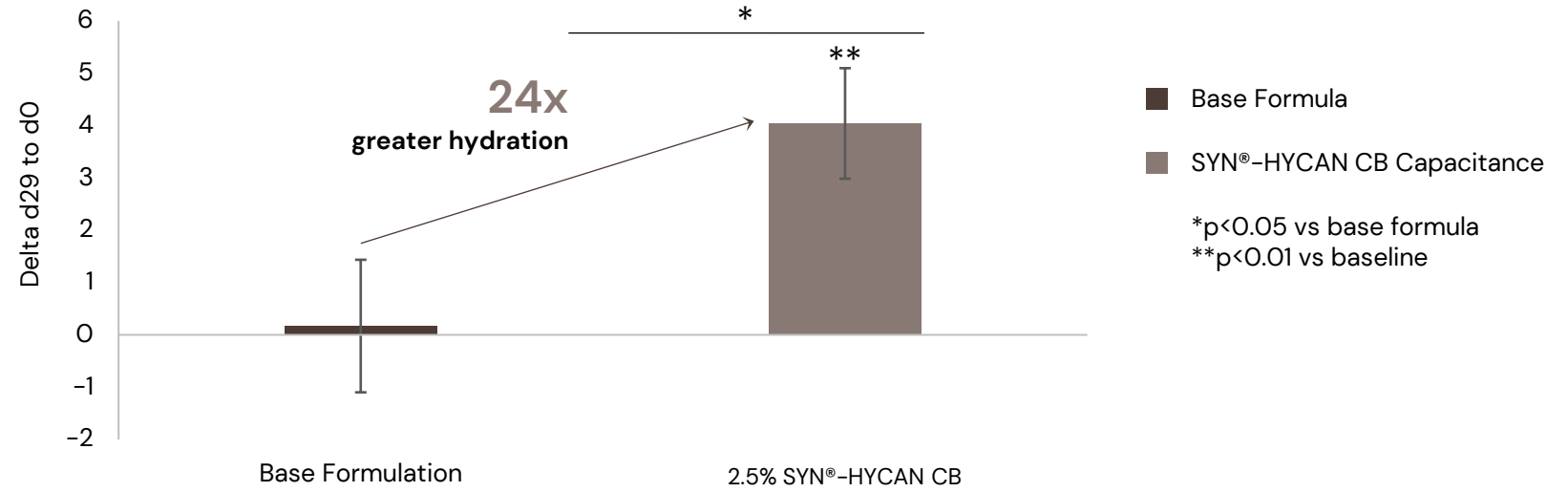
Skin Capacitance Assessment, Corneometer

in vivo

Instrumental Evaluation

Twice daily application for 1 month of a formulation with or without **2.5% SYN®-HYCAN CB** on full face. Caucasian female volunteers (30 per group) were between ages 40–60 with visible skin sagging on the face. Double-blind, placebo-controlled, randomized. Groups run in parallel. The device measures the dielectricity of the skin. Since dielectricity varies as a function of skin's water content, stratum corneum hydration can be measured. Test done on upper cheeks.

Corneometer values measured on cheekbone, mean of right and left side



Panelists using SYN®-HYCAN CB showed significant increase in skin hydration



Skin Firming and Remodelling

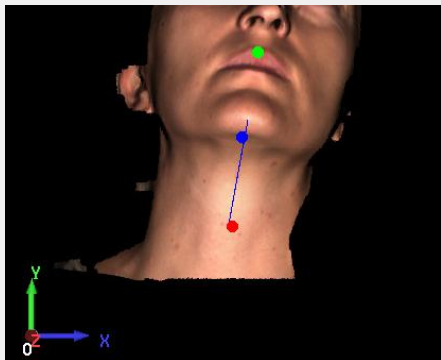
Skin Contour Assessment, PRIMOS Body, Dermscan, France

in vivo

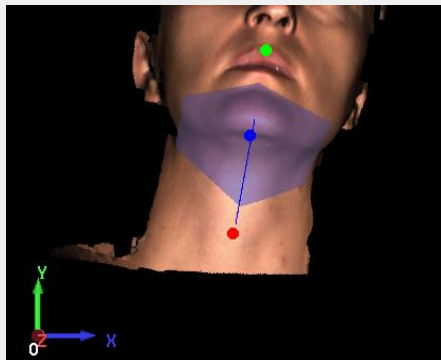
This device measures the change in the skin contour. A decrease in contour indicates a lifting effect.

Profile 1 and profile 2 are superposed and the distance observed between these two profiles was calculated.

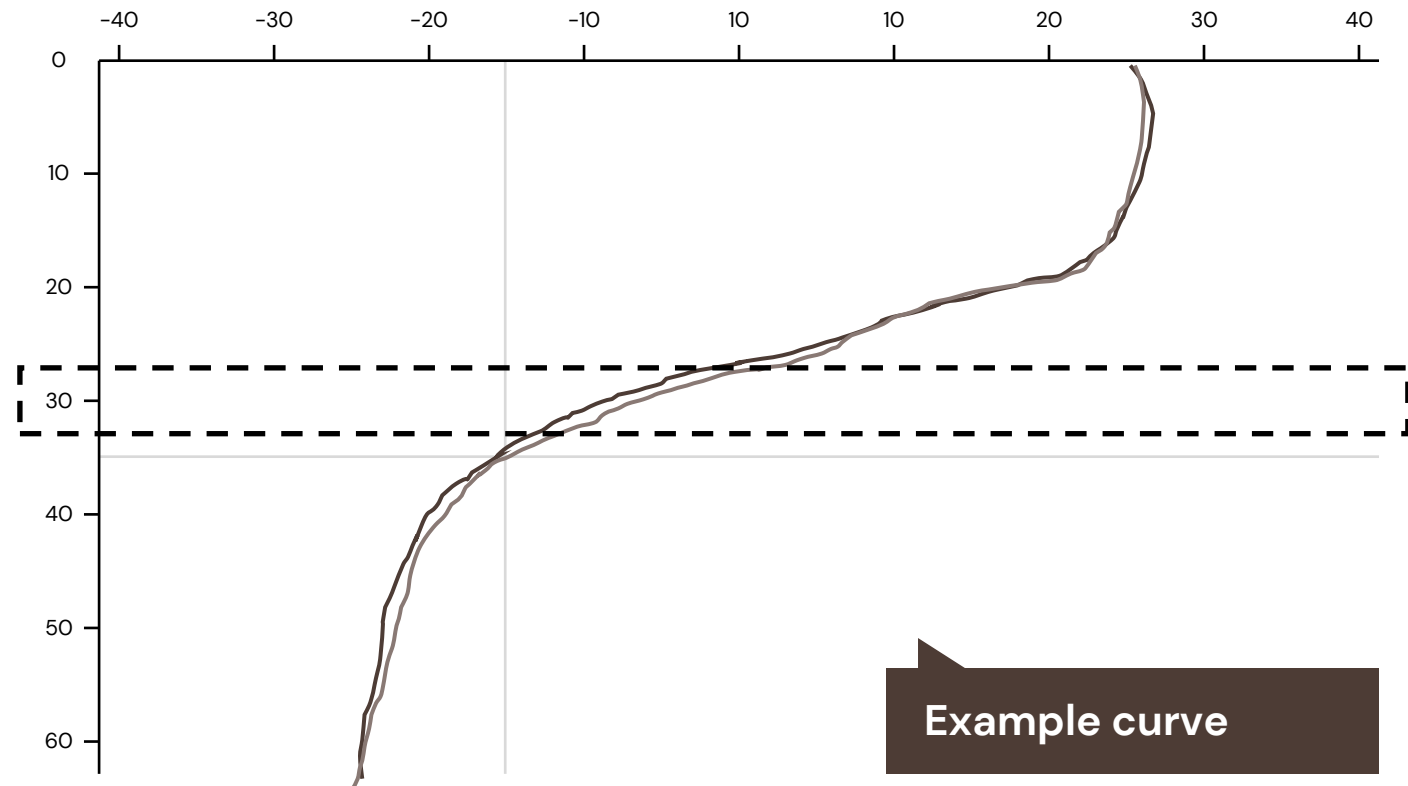
A decrease shows an improvement of this zone thus a less prominent (reduced) double chin.



Profile 1
D₀t₀ Image



Profile 2
D₁ Image



Example curve

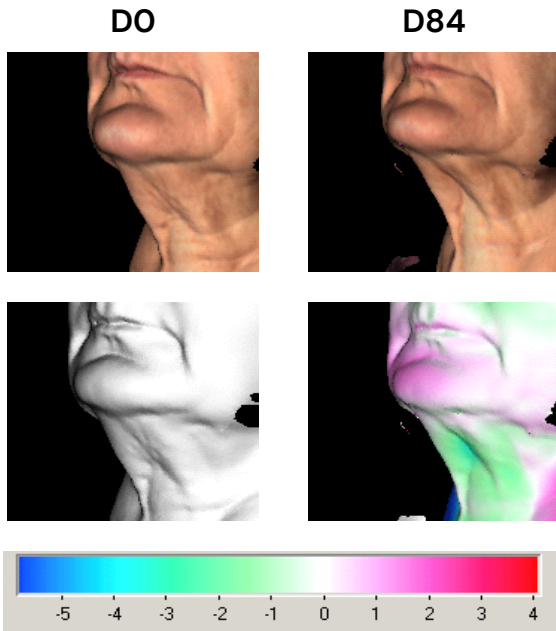
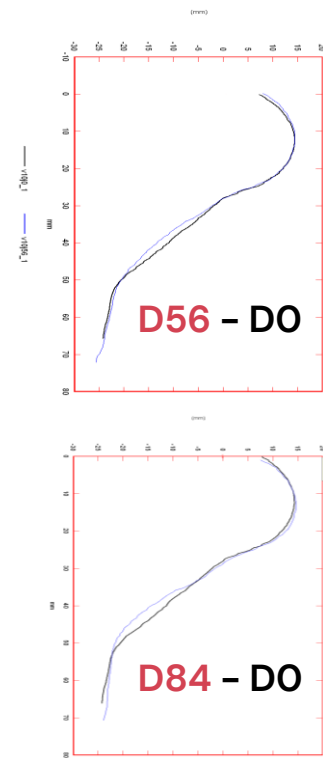
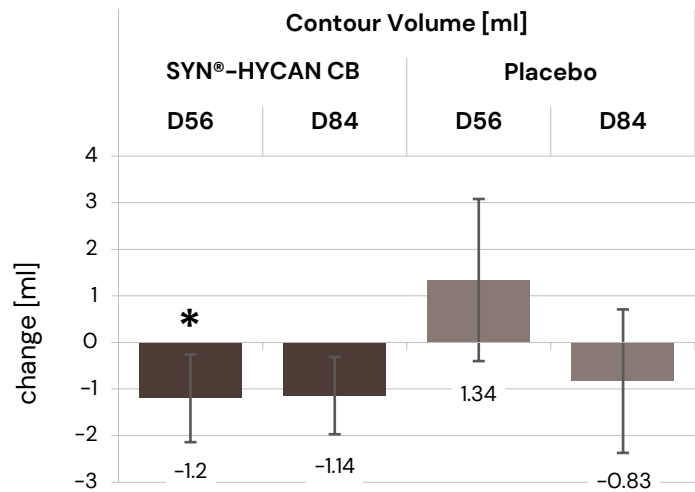
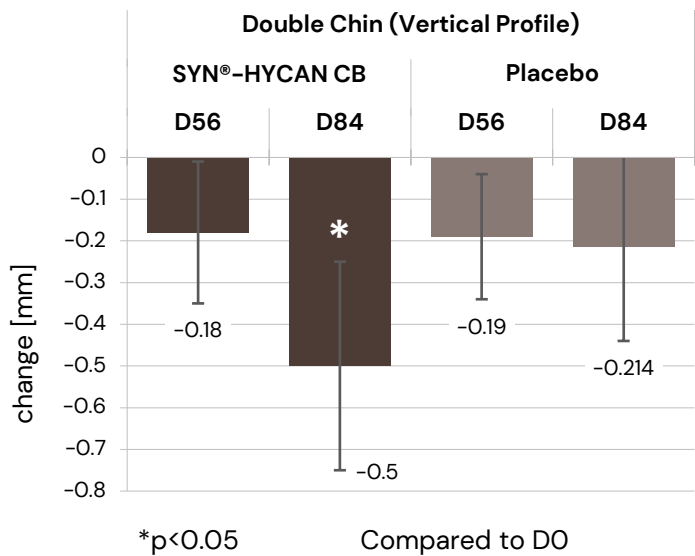
Skin Firming and Remodelling

Skin Contour Assessment, PRIMOS Body, Dermscan, France

in vivo

Instrumental Evaluation

Twice daily application for 3 months of a formulation with or without **2.5% SYN®-HYCAN CB** on face. Female volunteers (20 per group) were between ages 55-65 with visible skin sagging on the face. Double-blind, placebo-controlled. Groups run in parallel. Measurement of skin contour remodelling effect was done on neckline.



SYN®-HYCAN CB significantly decreases the double-chin profile by improved skin firmness. Visible face contour remodeling!

Visual assessment
volunteer #10, Firmness

Consumer-Perceivable Benefits

Volunteer Self-Evaluation

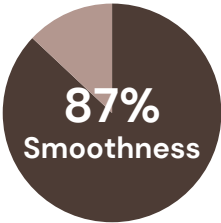
Panellist Self-Assessment – Subjective Evaluation – End of Study

Twice daily application of a formulation with **2.5% SYN®-HYCAN CB** on full face. 30 Caucasian female volunteers were between ages 40-60 with visible skin sagging on the face. Panellists asked to rate agreement with the following statements.

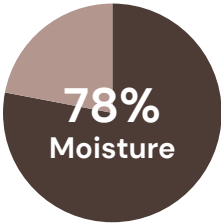
“ Using this product gave my skin...”



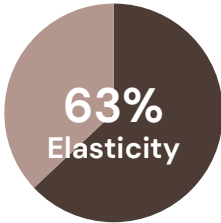
The product provides a supple skin feeling



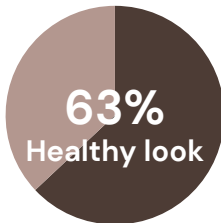
The product provides a smooth skin feeling



The product provides the skin with more moisture



The skin has more elasticity



The product gives the skin a healthy look



SYN®-HYCAN CB Summary of Benefits

dsm-firmenich 
new innovation

INCI: Tetradecyl Aminobutyroylvalylaminobutyric Urea Acetate

Unique product features

- Potent TGF-Beta activating peptide with proven HA synthesis action
- Proven to enhance skin firmness to support the new benefit of a “volumizing” effect
- Boosts production of dermal and epidermal hyaluronic acid, *in-vitro* and *ex-vivo*
- Boosts CD44, a key cellular receptor for hyaluronic acid
- Increases collagen 1, lumican and decorin levels, important for collagen organization & support*
- Outperforms competitive peptide technology in skin volumizing effect

Benefits

- Multi-zonal filling and firming effect on skin
- Skin is fuller and firmer in as early as 4 weeks
- Delivers substantial increase in skin hydration
- Skin is noticeably more supple, smooth and moisturized

Cosmetic applications

- Firming and volumizing skin care
- Regenerative night care
- Anti aging, anti-sagging
- Skin moisturizers

Suggested use level

- 2-5% SYN®-HYCAN CB for face, eye and neck applications



SYN[®]-HYCAN CB Formulation Guidelines

Solubility

- SYN[®]-HYCAN CB is miscible with water

Use level

- For skin care preparations, the addition of a concentration of 2–5% SYN[®]-HYCAN CB is recommended

Incorporation

- SYN[®]-HYCAN CB is easy to use, unpreserved, colorless and odorless
- SYN[®]-HYCAN CB can be incorporated into the aqueous phase of a cosmetic formulation
- SYN[®]-HYCAN CB can be processed either warm (for maximum 2 hours at 80°C) or cold.
The incorporation at the end of the production process at $T < 40^{\circ}\text{C}$ is still recommended to avoid unnecessary heating of the active

Compatibilities

- In general, SYN[®]-HYCAN CB shows a very good compatibility with all groups of raw materials like emulsifier systems, emollients and waxes, preservatives, hydrocolloids, sunscreens, detergents, and other commonly used substances, e.g. Phytantriol, for enhanced compound availability or boosting compound activity
- Recommended pH of the final formulation: 3.0 – 5.5, it can be adjusted with commonly used neutralizing agents
- Compatible with up to 50% ethanol (max. concentration tested)



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