

Active Beauty

Tightenyl™

The skin matrix Bio-lifter

Crafted by white technology



Givaudan

engage your senses

Ageing: the slow demolition of skin matrix pillars

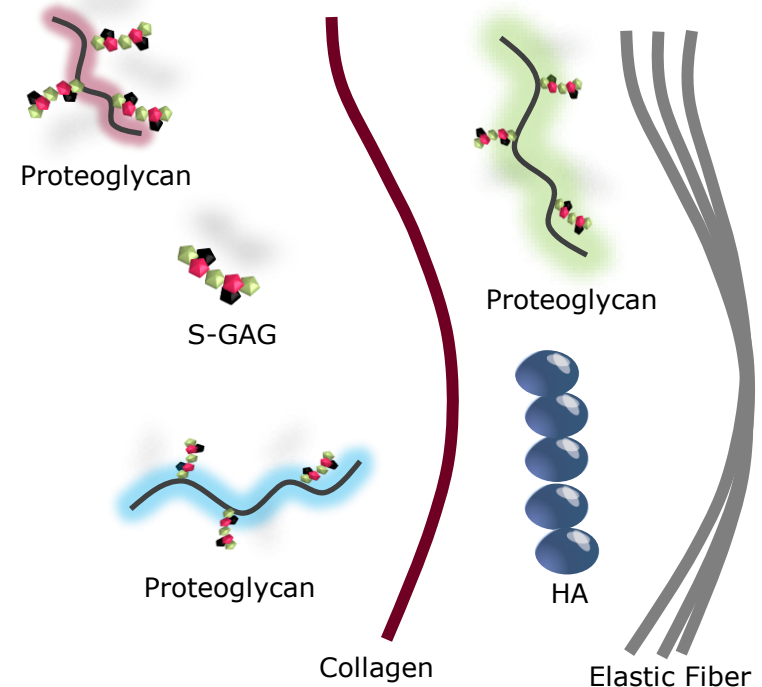
Skin matrix composition

Skin matrix is composed by:

- Polysaccharides (hyaluronic acid, sulfated glycosaminoglycans called S-GAGs)
- Proteins (collagens, elastin)
- Hybrid protein-sugar molecules (proteoglycans)

→ These macromolecules are essential in the Extra Cellular Matrix (ECM) to support the dermis-epidermis junction (DEJ)

→ They are mainly produced by fibroblasts



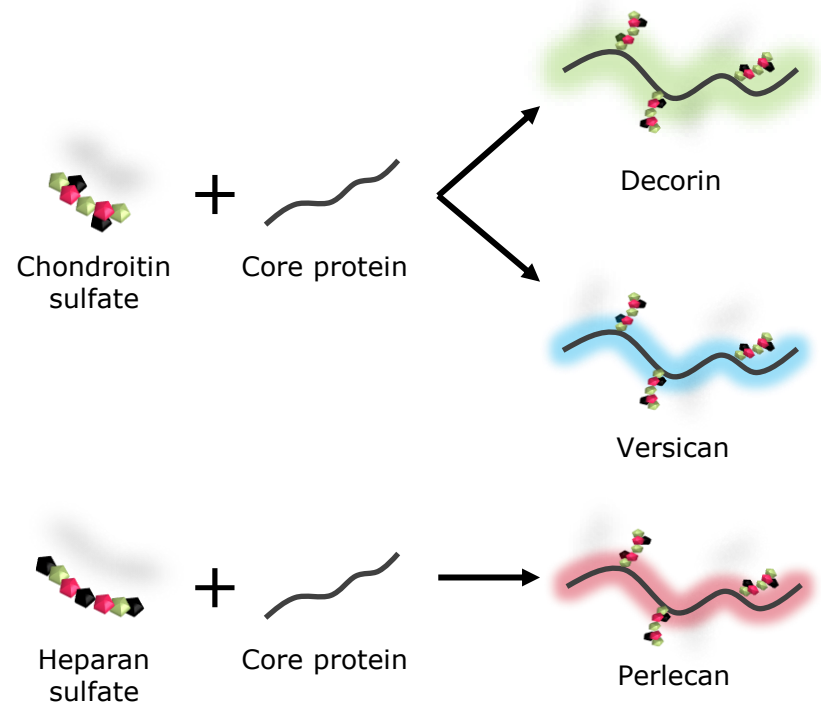
Skin matrix composition

Major S-GAGs are:

- Chondroitin sulfate
- Heparan sulfate

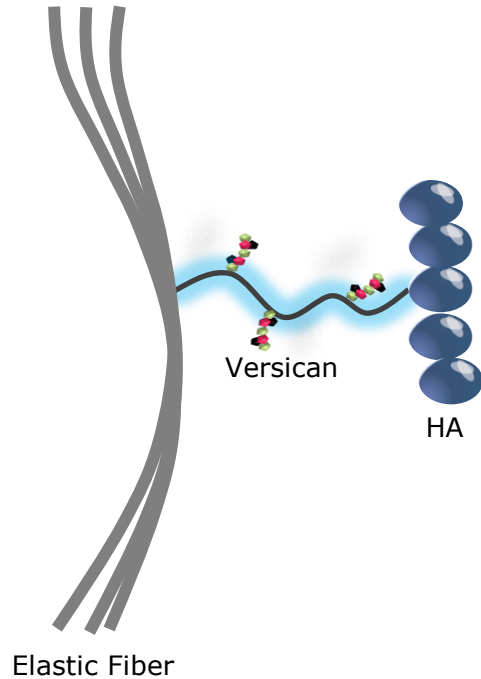
Major proteoglycans are:

- Versican: viscoelasticity of skin
- Perlecan: strengthening of DEJ
- Decorin: organization of collagen structure

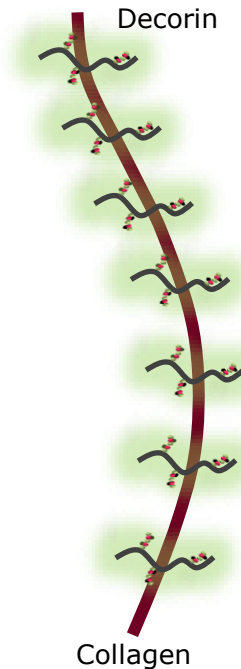


→ S-GAGs and their proteoglycans are key for ECM organization

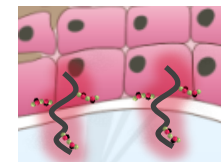
Interactions between proteoglycans and ECM proteins/sugars



Versican: control of elastic fibers orientation and link with HA



Decorin: control of collagen diameter and orientation



Perlecan

Perlecan: Essential component of DEJ to maintain its strength

S-GAGs and proteoglycans in cells functions

- Epidermis homeostasis
- Wound healing
- Hydration
- Control of inflammation
- Collagen fibrillogenesis
- Elastic fibers organization



S-GAGs and proteoglycans: healthy skin

¹ Journal of Structural Biology 164 (2008) 134–139

² Matrix Biol. 2005.

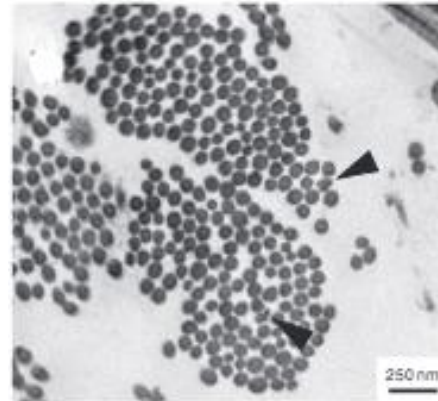
A lack of S-GAGs and proteoglycans induce:

- A disorganization in skin ECM leading to premature signs of aging
- A non homogenous size of collagen fibrils
- A poor 3D configuration of elastin

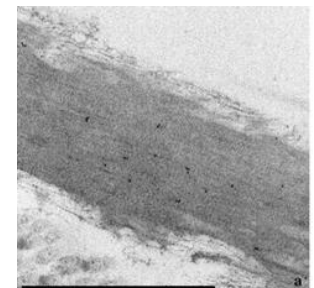
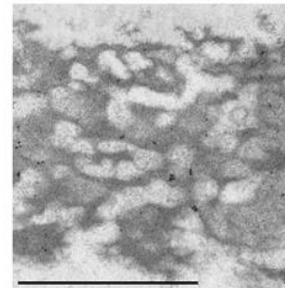
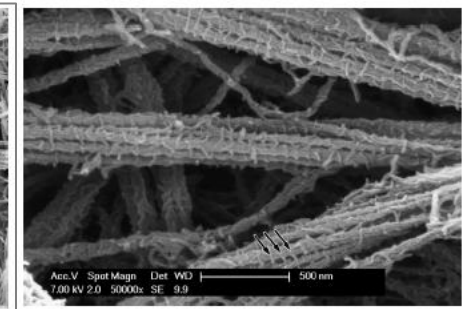
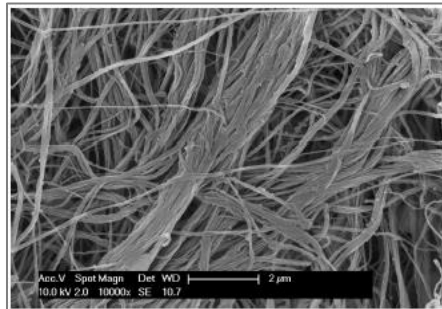
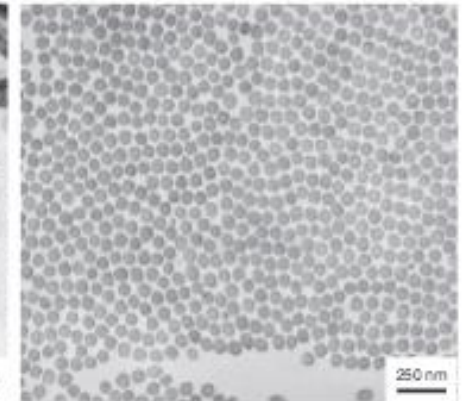
Collagen¹

→ The skin surface is wrinkled, even if there is still some collagen and elastin produced in the ECM

Lack of S-GAGs



Good level of S-GAGs



S-GAGs composition

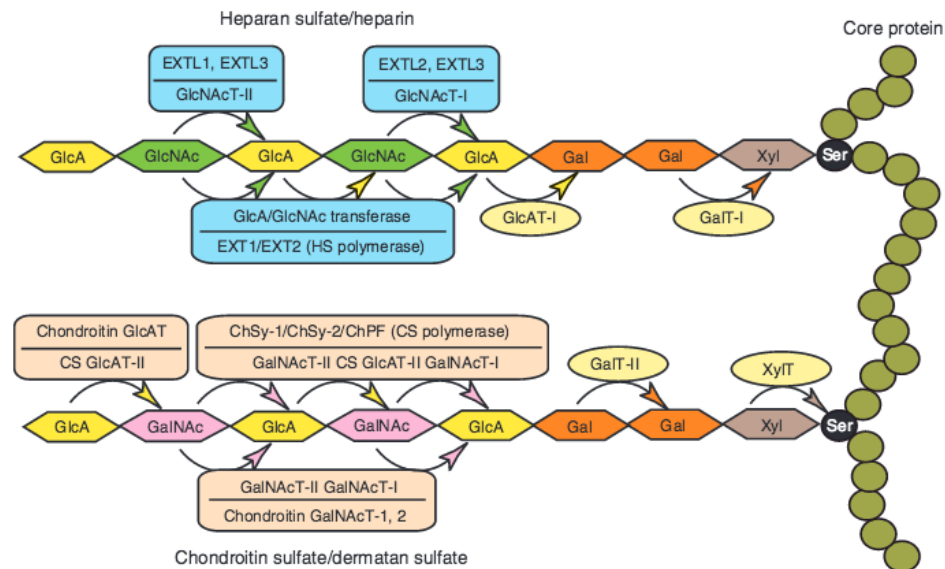
S-GAGs, in order to be synthesized, need:

- Precursors (N-Acetyl Glucosamine Phosphate and Glucuronic Acid)
- A source of sulfate

→ Upon aging, the availability of the sugar precursors is decreasing, inducing:

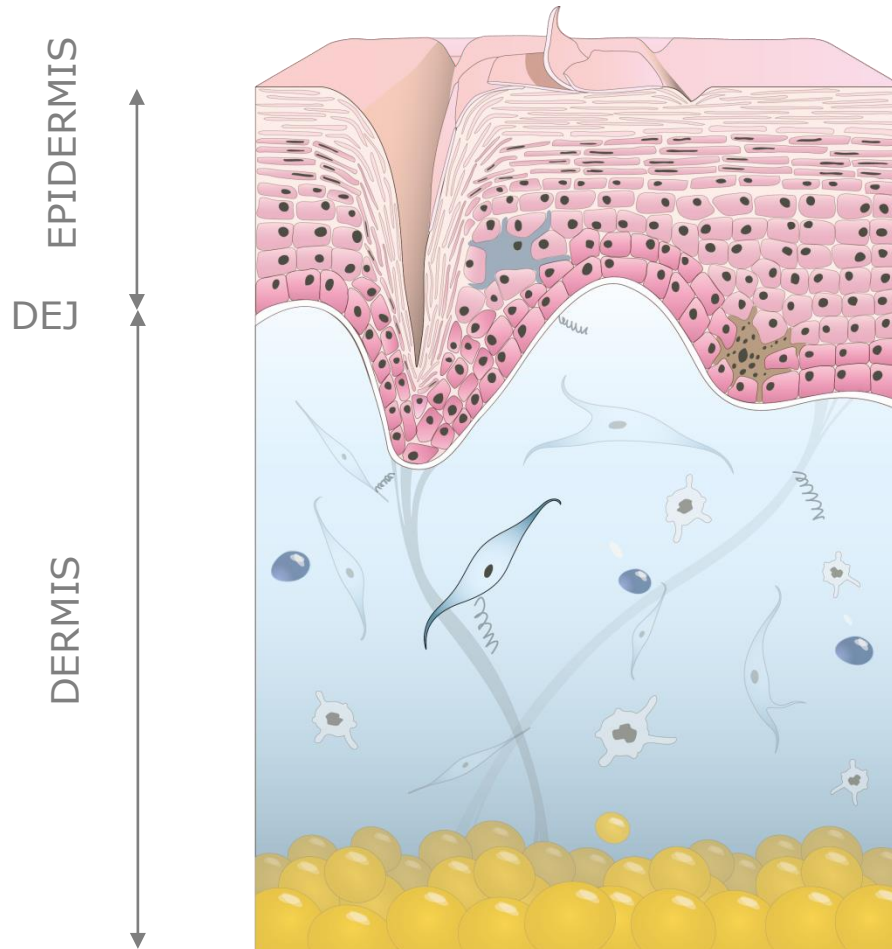
- Lower S-GAG production
- Less proteoglycans
- Loss of skin structure organization = aging

S-GAGs synthesis



Visual consequences of lack of S-GAG

The aging process for S-GAGs



- Less S-GAGs
- Less proteoglycans
- Poor skin matrix quality
- Visible aging

What can you do to avoid it?
A facelift? ...
...or an alternative?

Liftings worldwide

477,425

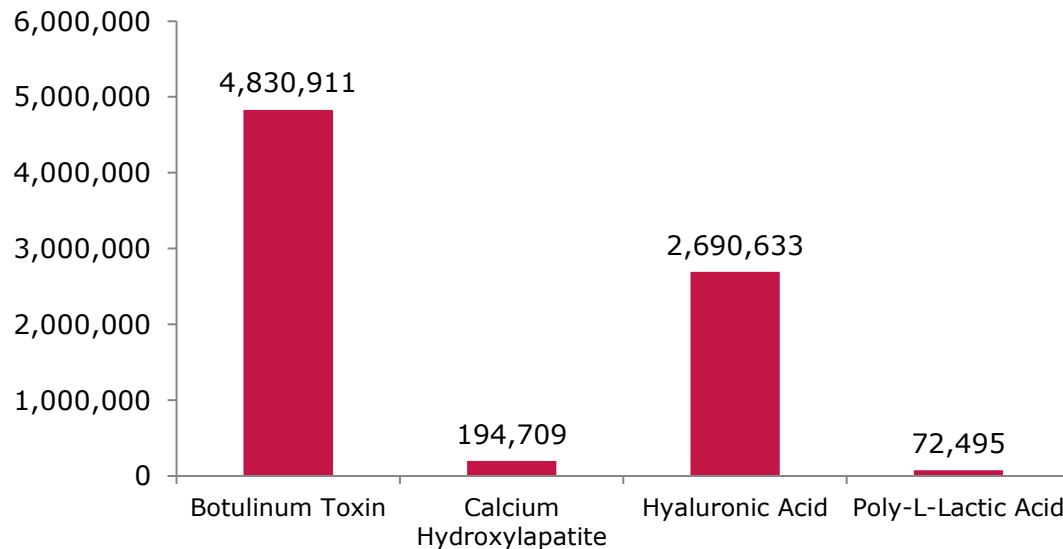
facelift procedures worldwide in 2014



Cosmetic Minimally-invasive procedures

7.788 million

in 2014



Consumer reviews

Why choosing plastic surgery?

Top 3 reasons

- « I want to look as young as I feel or better for my age »
- « I want to appear more attractive »
- « I feel more confident »



Positive feedback, but also negative

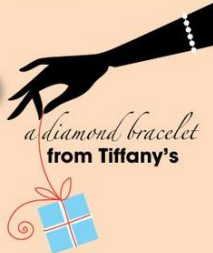
The two main reasons why people don't try cosmetic surgery:

- The fear
- The price



Are you willing to pay for it ?

The real cost of Cosmetic Surgery

Lose the man boobs (gynecomastia) \$3,013 or  70" flat-screen TV for your man cave	Get a Kardashian butt (clinical term is "buttock augmentation") or money down AND one year's lease on a car 	 meet twice weekly with a personal trainer for a year or Six-pack express (tummy tuck) \$5,130	 sponsor two children for an entire year through the Save The Children Foundation or Radiesse (wrinkle remover) \$650
\$6,231 or Be like Joan Rivers (facelift) a non-stop, round-trip flight to Rome + a week's stay at a five-star hotel Americans underwent 13.1 million cosmetic procedures in 2010, a 5% increase from the previous year.*	 or Shrink the schnoz (nose job) \$4,306 8 UNICEF water pumps for a third-world community, where the people will certainly not judge you or your nose	\$4,676 or Cover the dome (hair transplant) get a pair of endzone tickets to the 2012 Superbowl 	Botox \$373 or  10+ weeks of a daily venti-sized Starbucks latte fix
Boost the boobies (or "breast augmentation," if you want to be fancy) \$3,351 or  5 pairs of Christian Louboutin leather pumps	"Correct" your jaw like Bristol Palin (chin augmentation) \$2,000 or  a diamond bracelet from Tiffany's	\$475 Collagen injections or  weekly hour-long massages (plus tip) for a month	 But Wait, There's More! Opt for collagen that comes from a pig or a cow and save an average of \$7 per treatment! Suuu-weeeet! ~Barbara Bellisi

Tightenyl™
Rebuild the beauty pillars
And forget face lifting

Tightenyl™

An optimized and targeted composition

N-Acetyl-Glucosamine-6-Phosphate

- Precursor of S-GAGs

Glucuronic acid

- Precursor of S-GAGs

Magnesium Sulfate

- Source of sulfate necessary for sulfatation of S-GAGs

→ Tightenyl™ provides the essential elements to relaunch S-GAGs synthesis!



“deliver skin bioactivated precursors”

in vitro evaluations



Activation of the S-GAGs synthesis pathway (*transcriptomic*)

PROTOCOL:

Cells: HNDF (Human normal dermal fibroblasts)
from a 45 year old donor.

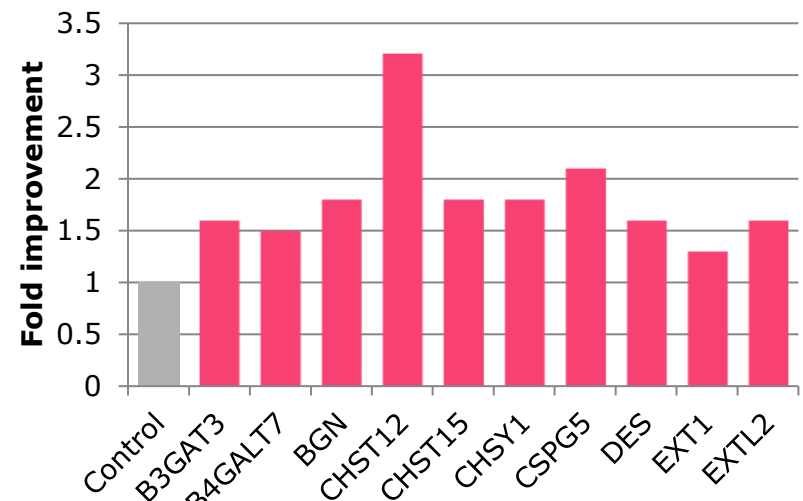
Treatment: Tightenyl™ at 0.6% and 1.2%.

Time: 18 hours.

Detection: mRNA expression quantified by q-RT-PCR.

→ **S-GAGs and proteoglycans** mRNA
synthesis incredibly improved by **1.5 fold** minimum
($p < 0.05$)

mRNA synthesis of S-GAGs and proteoglycans



Activation of cellular S-GAGs production (*in vitro*)

PROTOCOL:

Cells: HNF (Human normal fibroblasts) from 41 and 62 years old donors

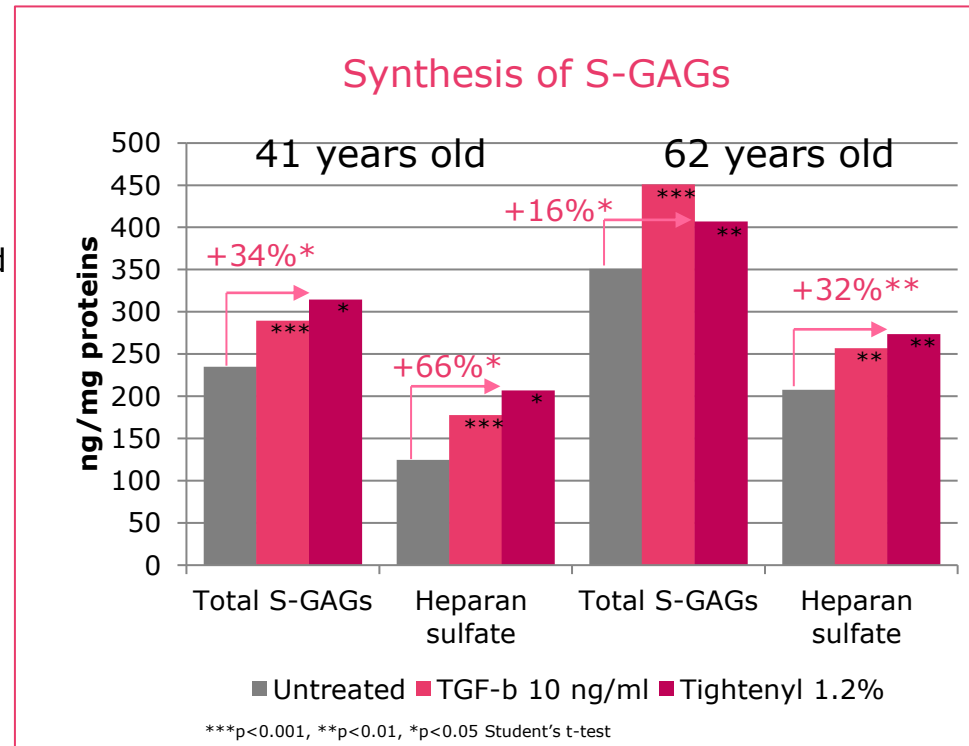
Treatment: 1.2% of Tightenyl™

Time: 3 days

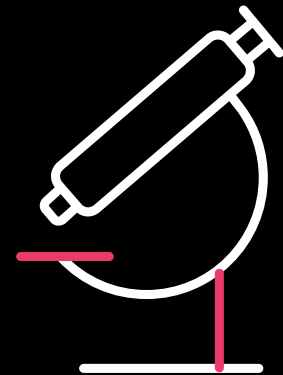
Detection: quantification of S-GAGs and N-sulfated GAGs by using specific kit assays

→ **+34%** and **+16%** of **S-GAGs** synthesis in mature/very mature fibroblasts respectively

→ **+66%** and **+32%** of **heparan sulfate** respectively.



ex vivo evaluations



Expression of chondroitin sulfate and heparan sulfate (*ex vivo*)

PROTOCOL:

Explants of a 45 year old donor.

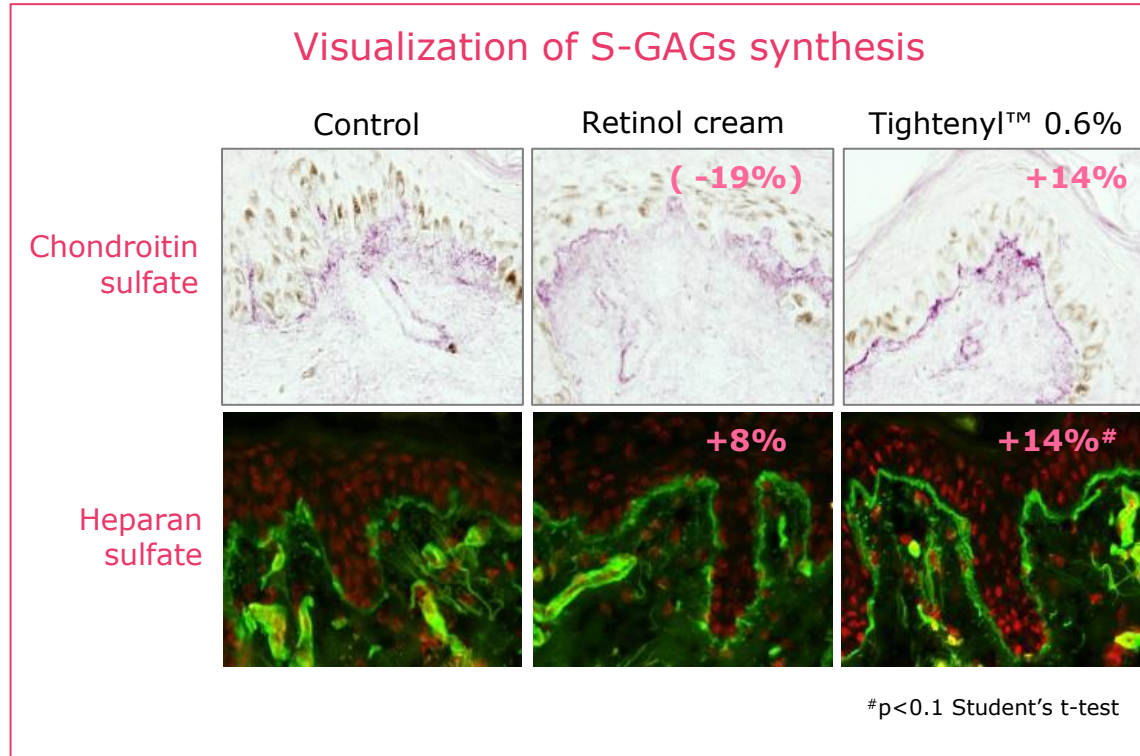
Treatment: topical application of Tightenyl™ at 0.6% or of a commercial cream containing Retinol

Time: 8 days.

Detection: immunostaining

→ **+14%** of heparan sulfate & chondroitin sulfate.

→ **Better results than Retinol!**



Expression of decorin, perlecan and versican (*ex vivo*)

PROTOCOL:

Explants of a 45 year old donor.

Treatment: topical application of Tightenyl™ at 0.6% or of a commercial cream containing Retinol

Time: 8 days.

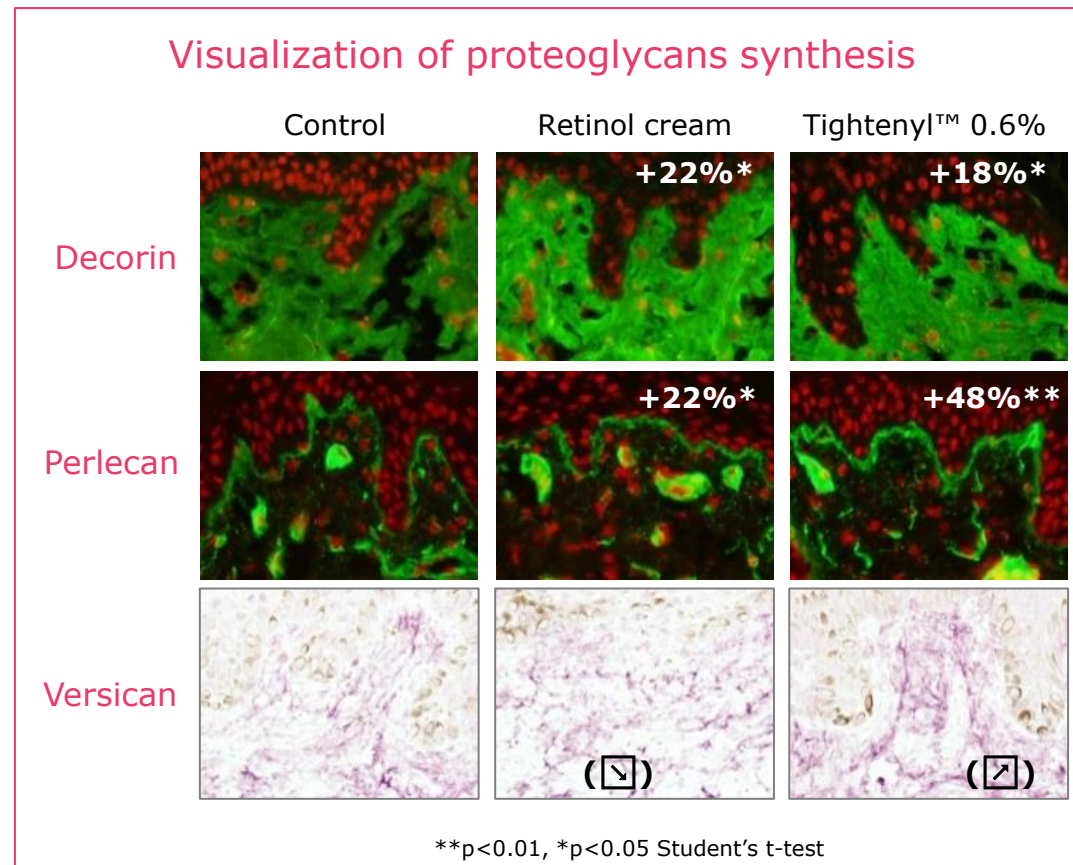
Detection: immunostaining (green for decorin & perlecan, pink for versican)

→ **Increased Versican synthesis.**

→ **+18% of decorin synthesis.**

→ **+48% of perlecan synthesis.**

→ **Twice better than Retinol!**



Improvement of skin morphology (*ex vivo*)

PROTOCOL:

Explantsofa 45 year old donor.

Treatment: topical application of Tightenyl™ at 0.6% or of a commercial cream containing Retinol

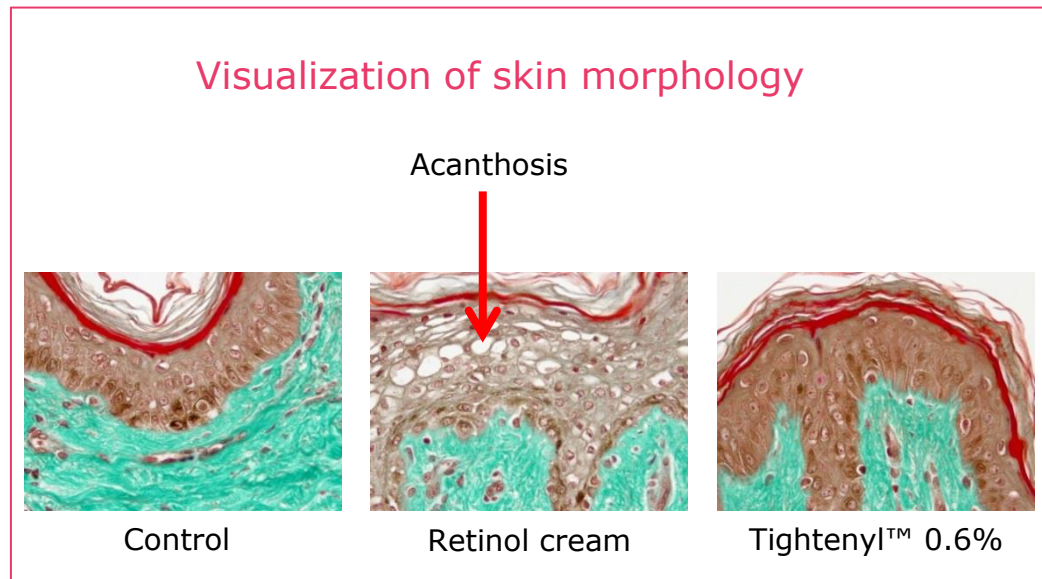
Time: 8 days.

Detection: staining using trichrome Masson technic

→ **Improved skin compactness** and DEJ after 8 days.

→ No irritation

→ Retinol is very irritating (Acanthosis)



Improvement of the dermis infrastructure (*ex vivo*) 1/2

Electron transmission microscopy

PROTOCOL:

Explants of a 45 year old donor.

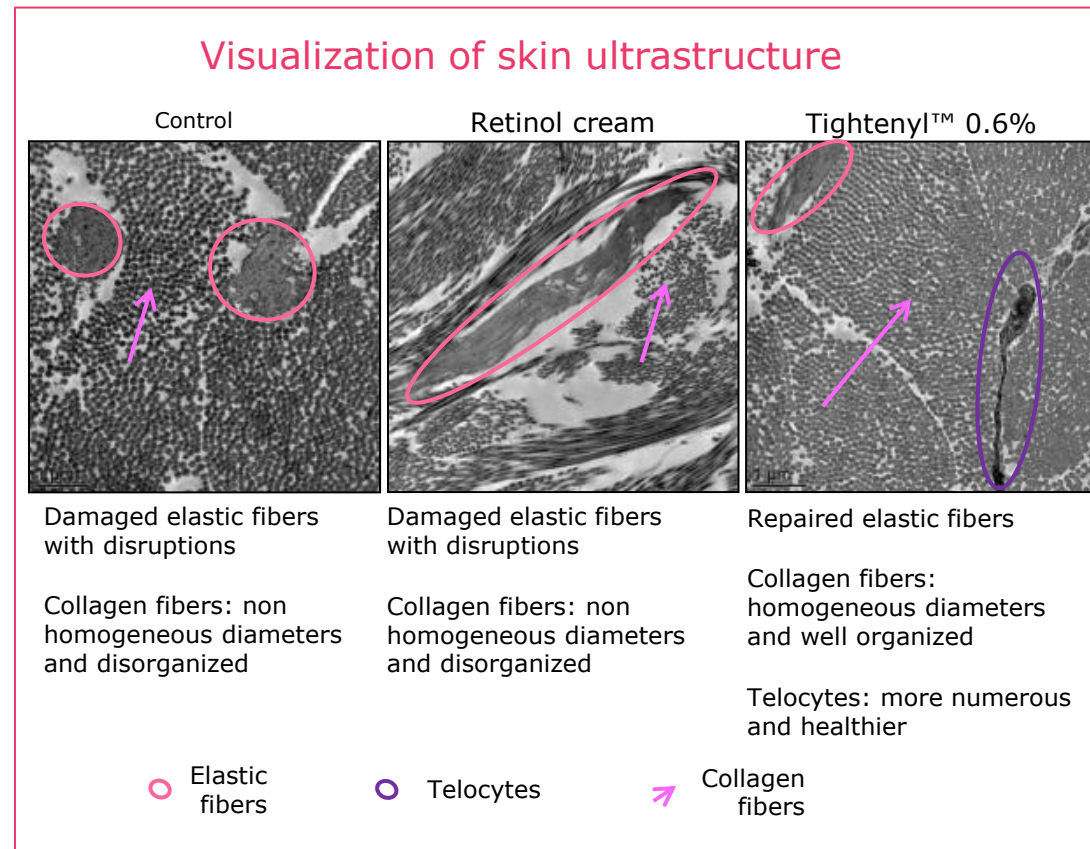
Treatment: topical application of Tightenyl™ at 0.6% or of a commercial cream containing Retinol

Time: 8 days.

Detection: electronic microscopy

With Tightenyl™:

- **Repaired elastic fibers.**
- Homogenous diameter of **collagen fibers**
- Better **skin matrix organization**
- Much better than Retinol!!



Improvement of the dermis infrastructure (*ex vivo*) 2/2

Biphoton microscopy

PROTOCOL:

Explants of a 45 year old donor.

Treatment: topical application of Tightenyl™ at 0.6% or of a commercial cream containing Retinol

Time: 8 days.

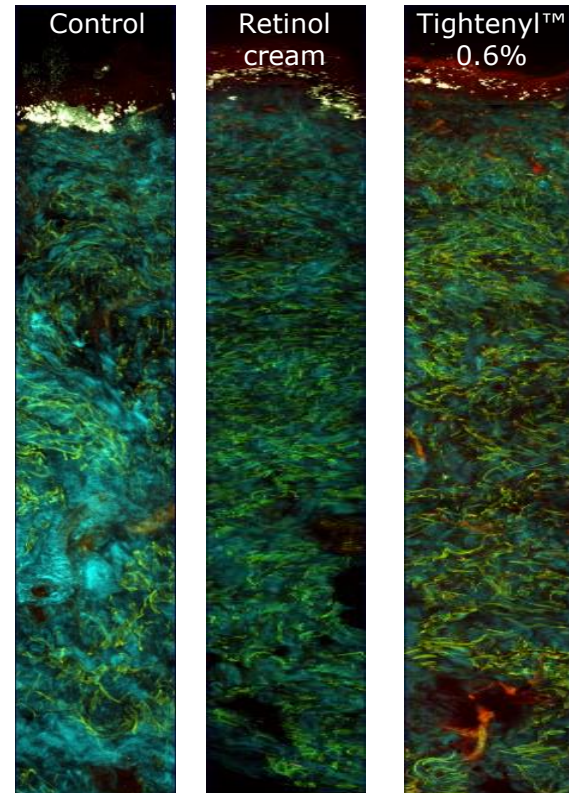
Detection: biphoton microscopy (green autofluorescence for elastin, blue for collagen)

→ **Reorganization of skin fibers.**

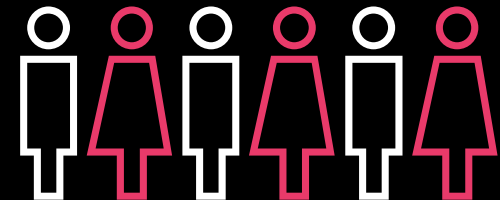
→ Redensification of skin EMC

→ Visible better effect than with Retinol cream.

Visualization of skin infrastructure



Clinical assessment



Clinical test conditions

Protocol

Single blind versus placebo

24 women, 47 to 65 years old

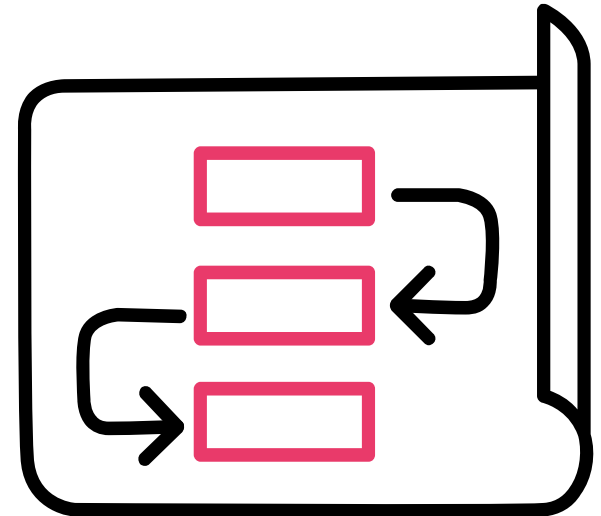
50% of them being menopausal

Test period: fall

Length: three months

Usage: application twice a day on the face of the placebo on one side, or placebo + 2% Tightenyl™ on the other side.

INCI: AQUA/WATER, OCTYLDODECYL NEOPENTANOATE, OCTYLDODECANOL, MYRISTYL MYRISTATE, ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER, SODIUM HYDROXIDE, PHENOXYETHANOL, METHYLPARABEN, ETHYLPARABEN, BUTYLPARABEN, PROPYLPARABEN, ISOBUTYLPARABEN (+/-) TIGHTENYL™ 2%



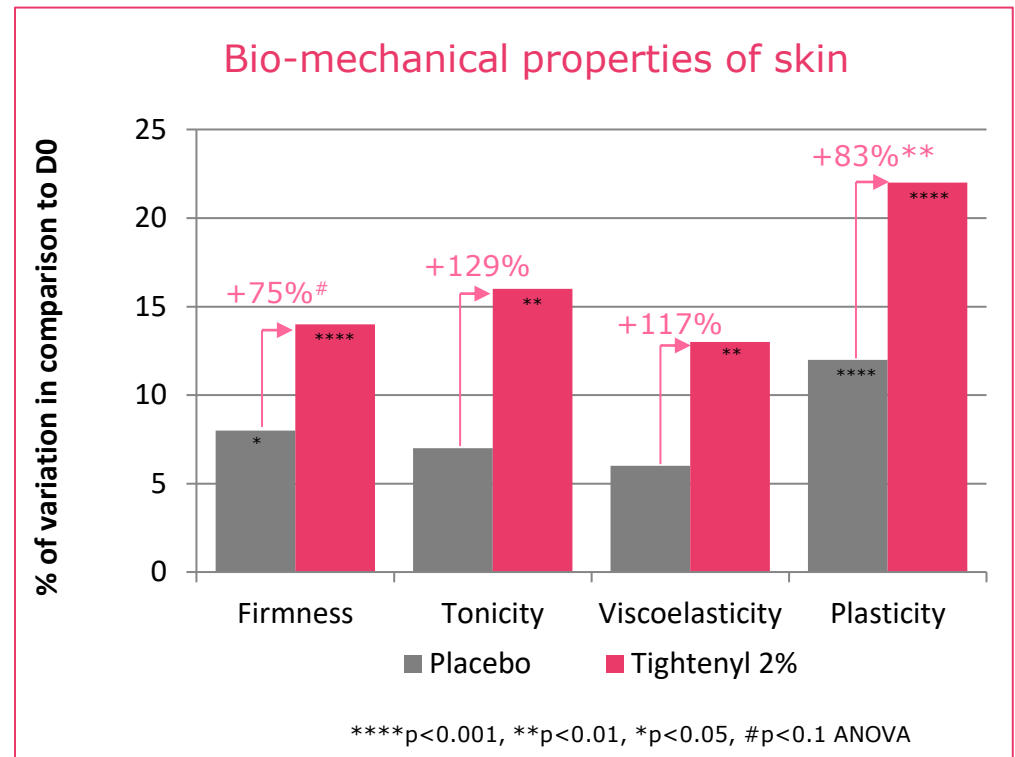
Fast improvement of mechanical properties (clinical) (cutometer)

PROTOCOL:

Measurement of the bio-mechanical properties of the skin after 15 days using a cutometer

In **only 15 days!!!!**

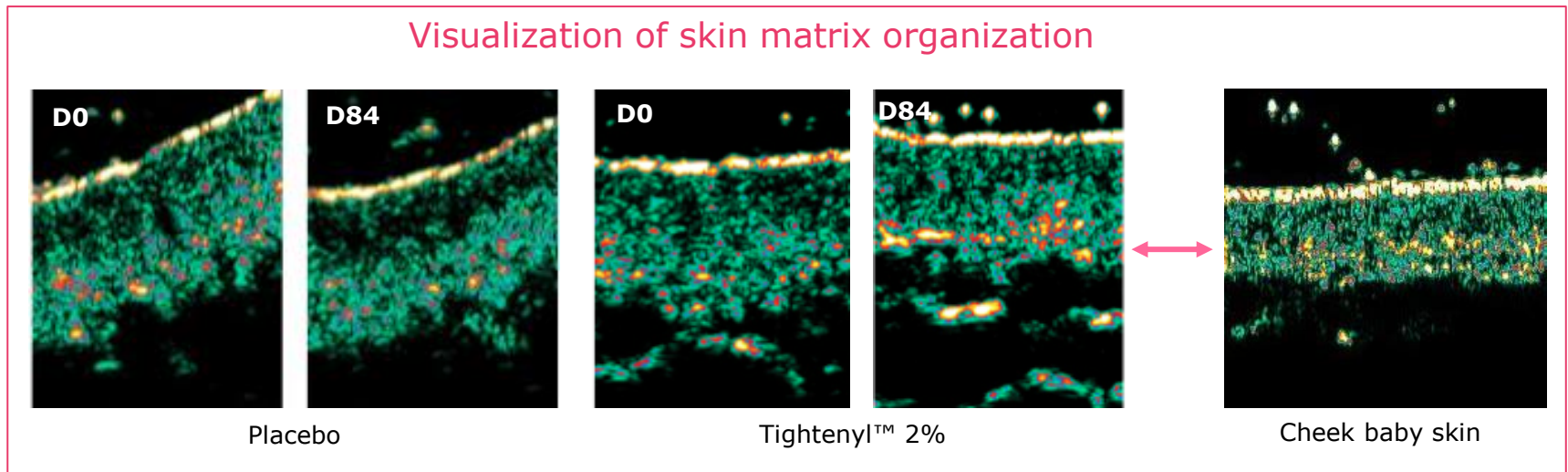
- **+75%** of skin firmness (Uf)
- **+129%** of skin tonicity (Ur)
- **+117%** of skin viscoelasticity (Uv/Ue)
- **+83%** of skin plasticity (Uv)



Back to a baby skin quality (clinical) (echography)

PROTOCOL:

Evaluation of skin matrix redensification after three months by echography.



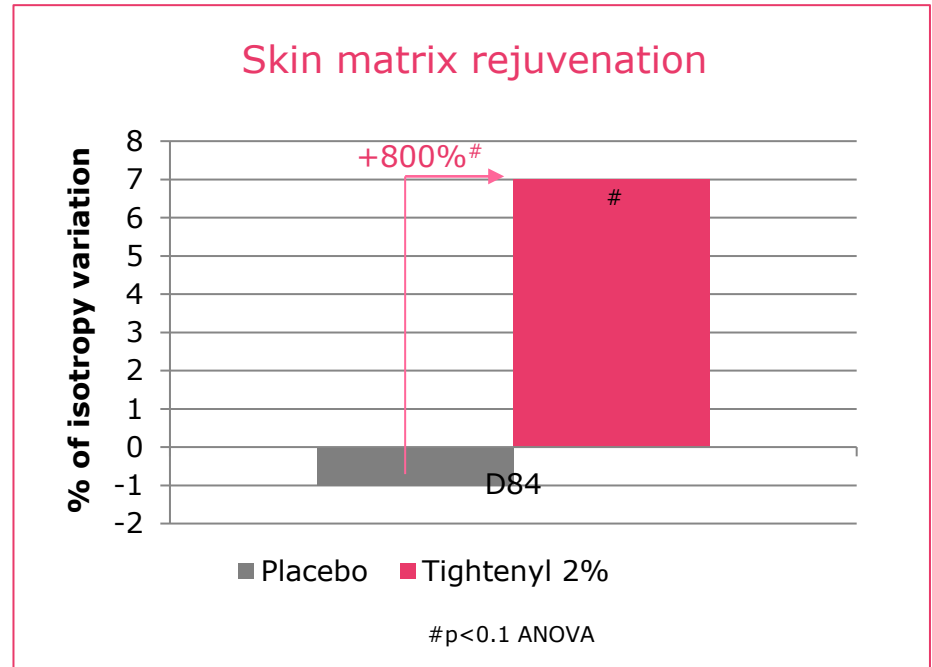
- Better skin density (less black visible)
- Skin matrix almost equivalent to baby skin
- The placebo degrades the matrix visibly

Biolifting effect (clinical) 1/2 (Primos 3D)

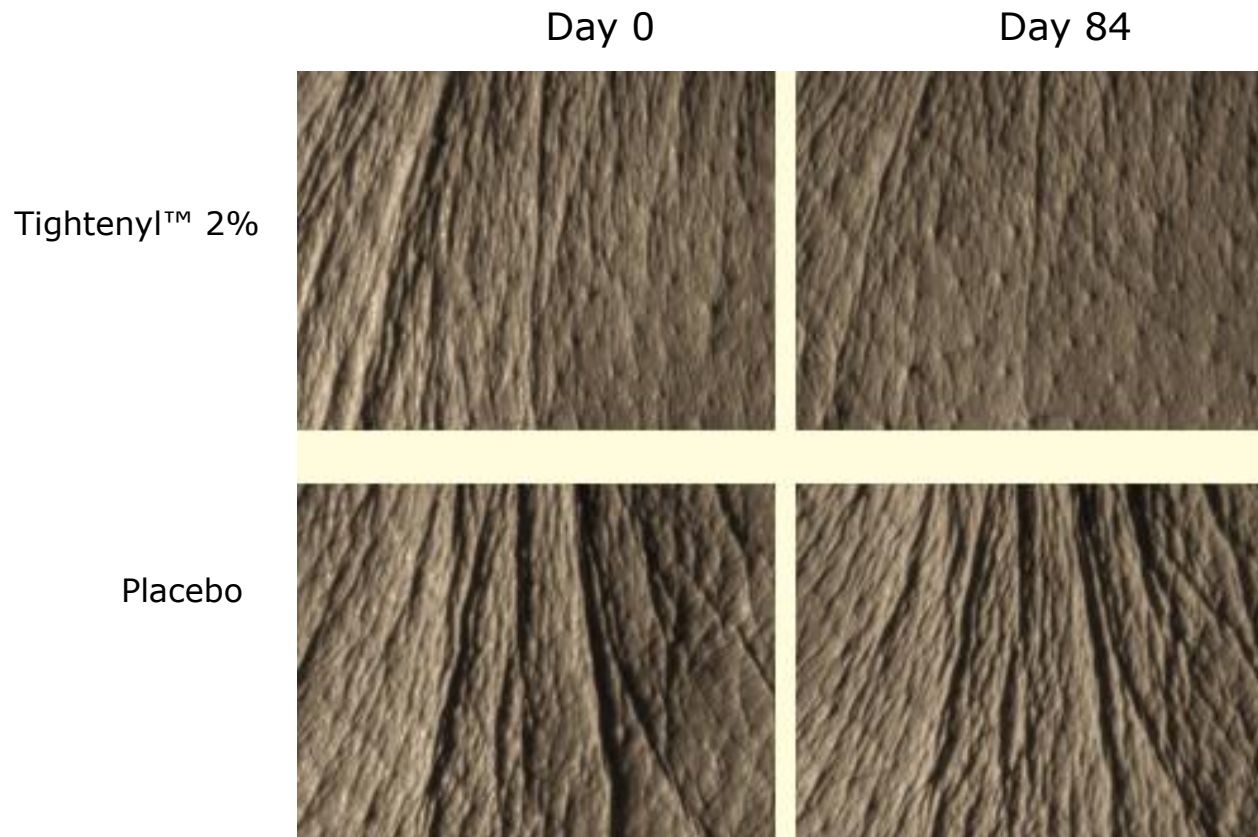
PROTOCOL:

Measurement of skin isotropy after three months using a PRIMOS 3D.

→ **+800%** of skin isotropy
→ The **skin matrix is rejuvenated**



Biolifting effect (clinical) 2/2 (silicone replica)



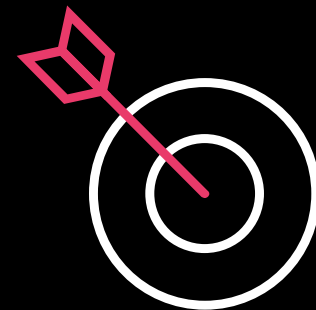
Visible benefit

Macro pictures after 3 months



Results: The results are outstanding by using 2% Tightenyl™ after 3 months. The skin is visibly smoothed, meaning that the dermis structure is better organized.

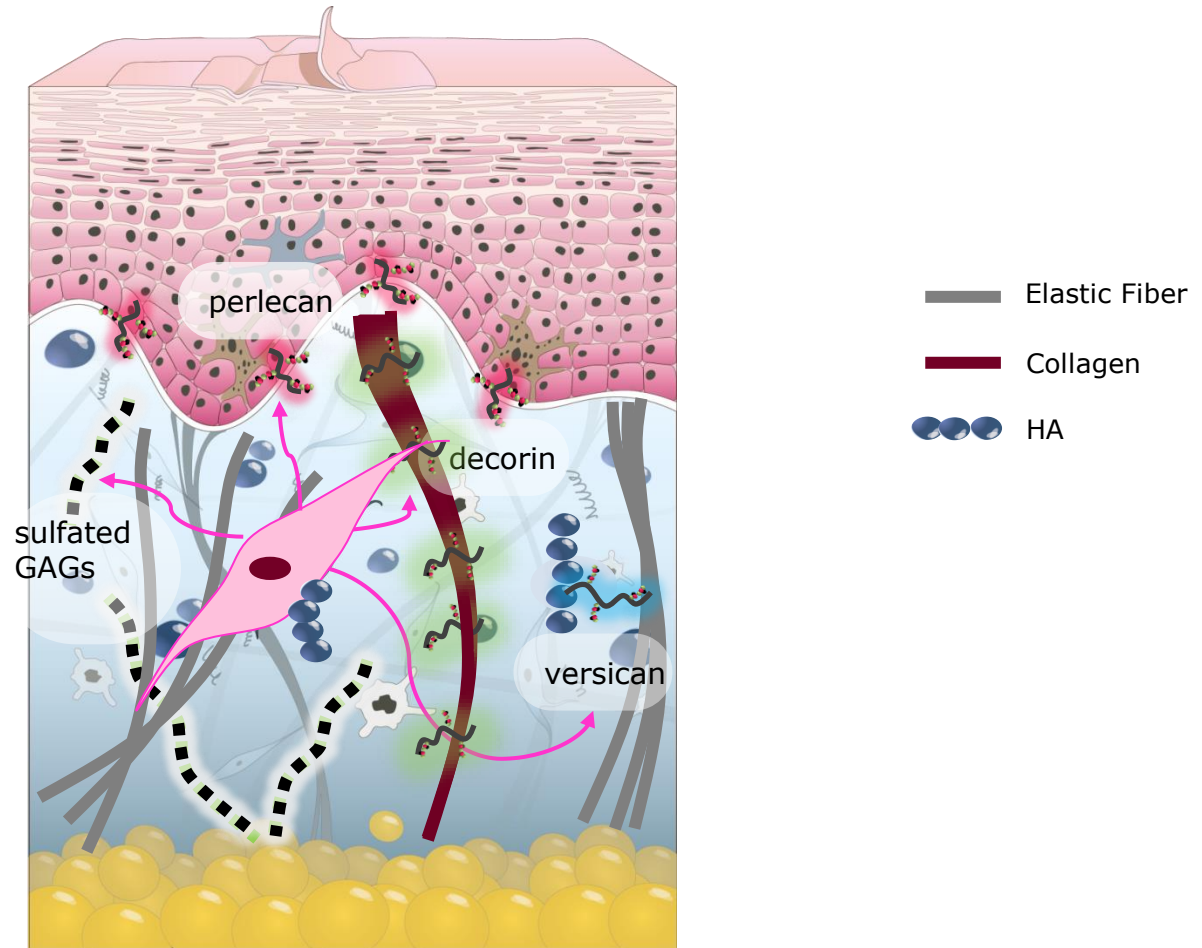
Summary



Tightenyl™ mode of action

A fast action on S-GAGs synthesis for skin reorganization

Tightenyl™



Main claims

Offering alternatives to surgery

- Skin bio-lifting
- Skin sagging prevention
- Anti-ageing
- Skin firming
- V-shape restructuring
- Face contour remodeling



Applications

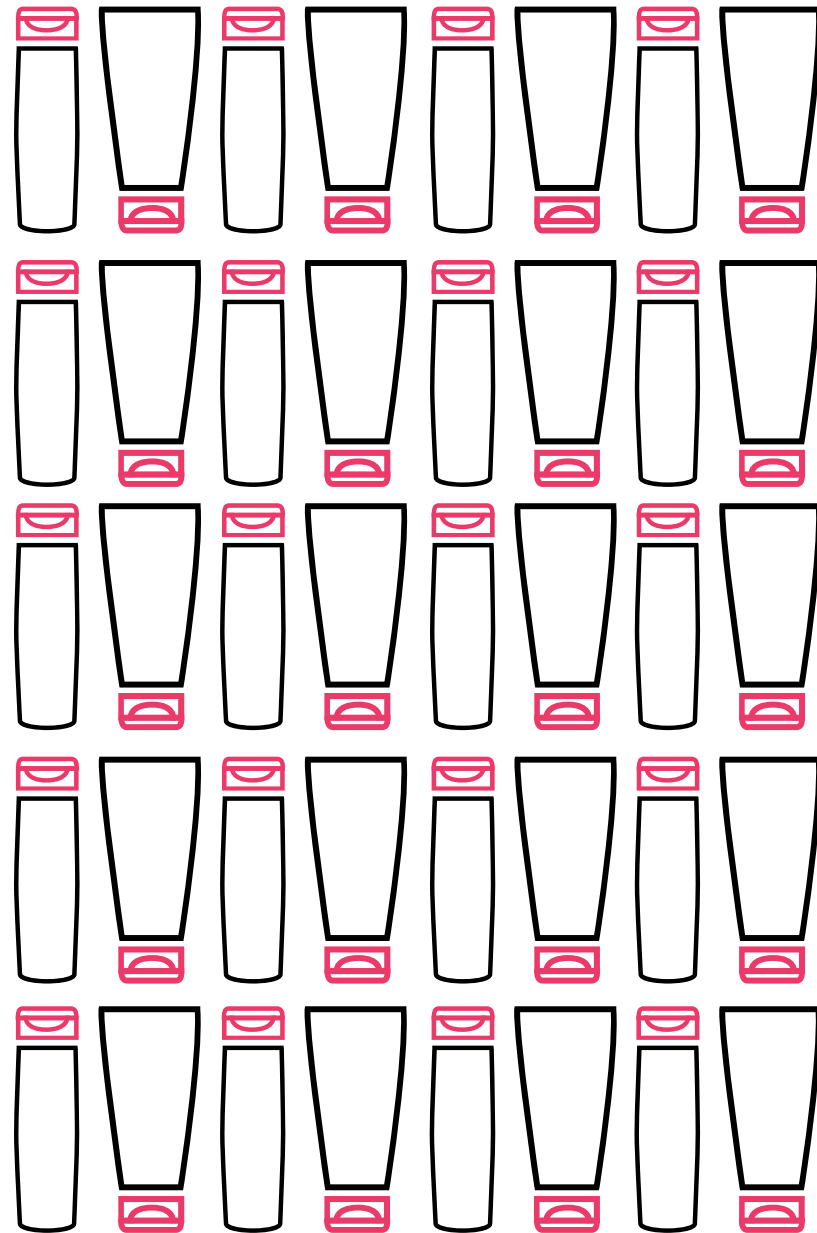
Youth is in the consumers' hands

Face care

- Replacement of retinol
- Anti ageing creams
- Face lifting serums
- Intensive treatments for facial rejuvenation
- Night and day creams to firm the skin
- Active anti-aging sprays
- Multifunctional creams (BB or CC creams)
- Dermocosmetic products

"Needle-free" product line

(in connection with Neodermyl™, Stimulhyal)



Technical information

Tightenyl™

INCI

Glycerin (and) Water (and) Disodium Acetyl Glucosamine Phosphate (and) Sodium Glucuronate (and) Magnesium Sulfate

Origin

Biotech

Preservation None

Appearance Pale yellow liquid

Solubility Water soluble

Dosage 0.6 - 2%

Processing

Can be added at the end of the formulation process under stirring or homogenizing. Can be heated for a short time with the water phase of formulation. Formulate at temperature below 50°C, and final pH below 6.0.

Compliance



"Rebuild the beauty pillars"

Thank you.

Active Beauty

global.cosmetic@givaudan.com