

Matrixyl™



the effective
alternative
for erasing
wrinkles



Matrixyl™

the effective alternative for
erasing wrinkles and stimulating
the dermal matrix

Matrixyl™ - how it works

As we get older, the lack of collagen in the dermis is thought to be the major reason for wrinkle formation, so if the skin can be stimulated into synthesising more collagen, we should be able to reverse the trend and diminish facial wrinkles.

The active molecule in Matrixyl™ is **Micro-collagen™**, a peptide which, when applied to the skin surface via a cream containing Matrixyl™ penetrates the skin, reaching the fibroblast cells. Here it incites the cells to synthesise the molecules of connective tissue, the skin 'matrix', such as collagen and glycosaminoglycans.

Before



After

Why Micro-collagen™?

Matrixyl™ contains as the active ingredient a synthetic, miniature fragment of the skin's most abundant protein, collagen. This fragment, a pentapeptide composed of the amino acids Lysine, Threonine and Serine, is made lipophilic by the attachment of palmitic acid to the first amino acid, which leads to the sequence Pal-Lys-Thr-Thr-Lys-Ser (Pal-KTTKS).

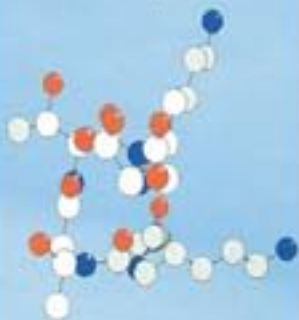
Mimicking nature's tissue regenerating processes in which this fragment plays the role of messenger, Micro-collagen™ acts specifically on the cells of the dermis, signalling them to synthesise the material necessary for padding the skin: connective tissue composed of proteins (collagen I, III, IV) and polysaccharides (glucosaminoglycans, hyaluronic acid).

In particular, collagen IV is important for the repair of the epidermal-dermal junction (EDJ) that maintains skin elasticity and profile.

The concept of 'micro' is also reflected in the minute amounts of Micro-collagen™ needed to obtain cellular response: 3ppm (mg per kg) suffice to activate the fibroblasts in the skin. Thus, Micro-collagen™:

- is a synthetically obtained micro-fragment of natural collagen
- initiates the stimulation of collagen synthesis
- and is, therefore, able to replace collagen injection or other devices and methods in the treatment of wrinkles.

Micro-collagen™



‘with Matrixyl™ I can really see the improvement in my wrinkles’

Matrixyl™ - the evidence - an industry first

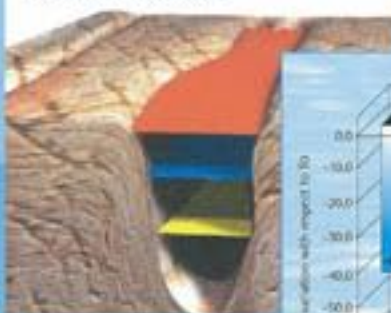
In vitro and *ex vivo* studies show conclusively that Micro-collagen™, the active ingredient of Matrixyl™, does induce cells to synthesise collagen and GAGs (glycosaminoglycans). Studies were then carried out on 35 volunteers over a six month period - an industry first - with intermediate results analysed after two and four months. The data confirmed that improvement of the skin is almost linear with time.

The same applies with self-assessment - the percentage of volunteers who endorsed the statement "The product improves wrinkles", increases with time, parallel to the results of the physical measurements.

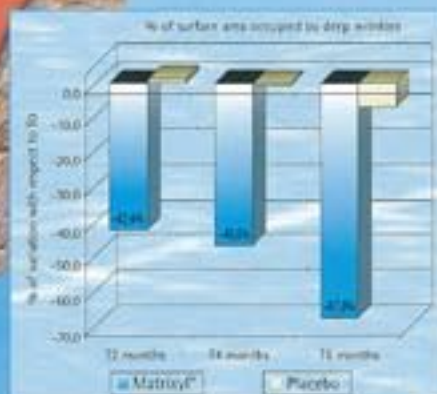
Claim substantiation

Within the context of that study, the following parameters have been retained: wrinkle surface - wrinkle volume - wrinkle density - skin roughness - wrinkle depth.

The wrinkle surface



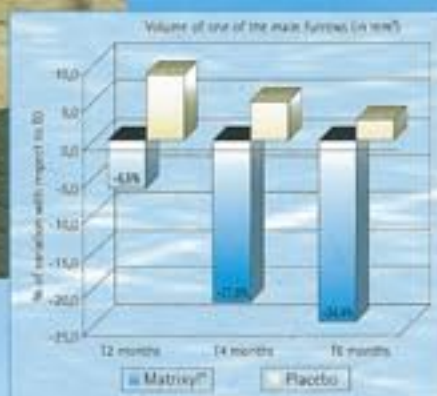
Parameter: % of surface (yellow zone) occupied with deep wrinkles (>200µm)



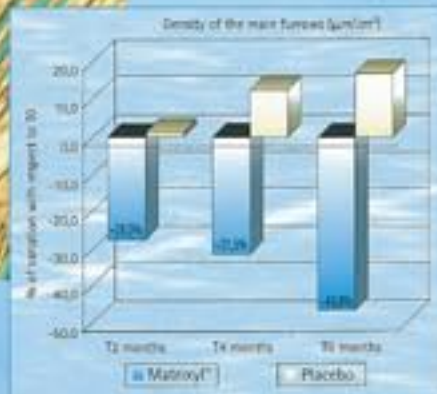
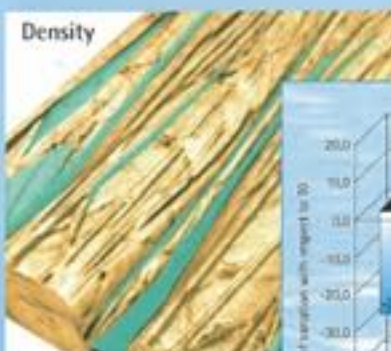
The wrinkle volume



Parameter: volume of one of the main wrinkles (mm³)



Density



Matrixyl™ - the new benchmark

A comparison study was carried out with Matrixyl™ cream against a commercial cream containing 5% Vitamin C. Vitamin C is currently used as the benchmark, by virtue of its own capability to stimulate collagen synthesis. However, Vitamin C is difficult to formulate and stabilise in cosmetic formulas.

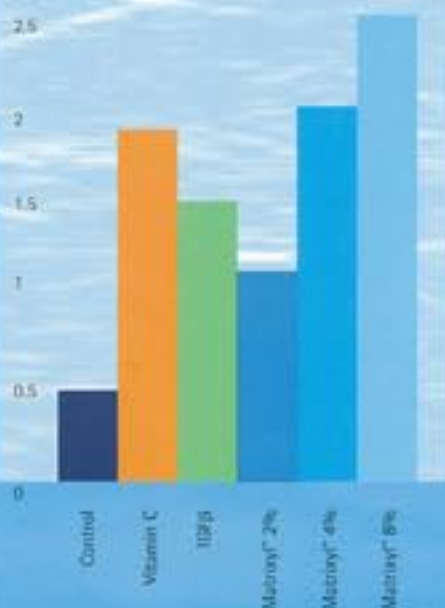
We have carried out a number of studies, all of which confirmed the indisputable efficacy of Matrixyl™ and the active ingredient Micro-collagen™:

- *in vitro* on human fibroblasts
- *ex vivo* on human full thickness skin biopsies
- *in vivo* on human volunteers over 2/4/6 months.

Claim substantiation *in vitro* carried out on human fibroblasts in culture

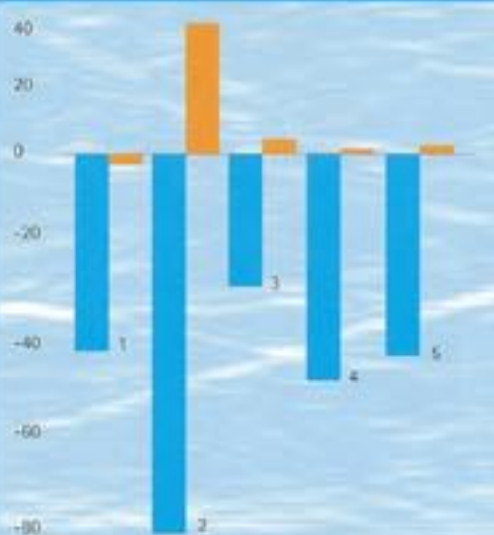
Stimulation of the synthesis of soluble collagen IV

OD/mm²



4ppm of pure Micro-collagen™ are as effective as 20ppm of pure vitamin C

Results after 6 months treatment



Demonstration of the antiwrinkle activity of Matrixyl™ compared to a marketed cream containing vitamin C.

Protocol: cream with 3% Matrixyl™ - cream containing 5% Vitamin C - 2 daily applications of each product during 6 months - 10 people - hemifacial application.

The profilometric measurements are obtained from the analysis of the prints taken in the eye contour area.

1 % of surface occupied with wrinkles (>200µm)

2 Density of wrinkles

3 Roughness

4 Volume of the main wrinkle

5 Average depth of main wrinkle

■ Matrixyl™ 3%

■ Vitamin C 5%

The difference of the variations observed between the Matrixyl™ side and the vitamin C side is highly significant.

after 4 months the wrinkles diminished
on my face

Further tests

In vitro

Katayama et al (1991) investigated the stimulating activity of the collagen fragment Lys-Thr-Thr-Lys-Ser on fibroblasts and found that this peptide increased the synthesis of collagen I and III, but also of **Fibronectin**, another matrix molecule of the connective tissue.

We then studied the synthesis of glycosaminoglycans (GAGs) in human skin fibroblasts and their stimulation by small amounts of **Micro-collagen™**. The rate of synthesis of GAGs is increased by 267% over the basic rate by 2% Matrixyl™.

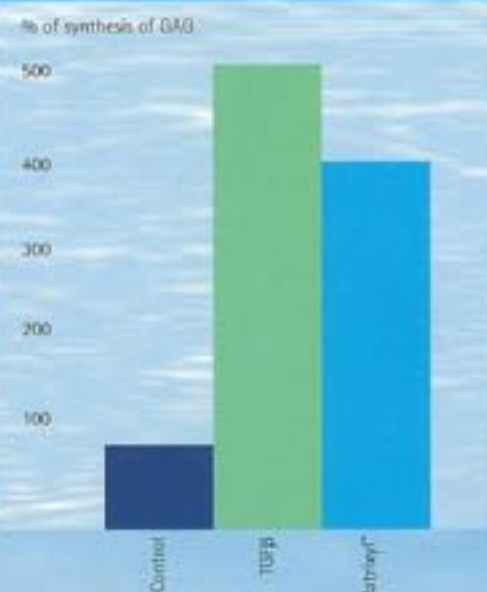
Ex vivo

The repair effect of **Micro-collagen™** on full thickness skin was proven in a biopsy model: the incorporation of radiolabelled proline into collagen molecules was measured against the concentration of the peptide in comparison to Vitamin C and TGFβ as controls.

In vivo

Clinical examinations by a dermatologist confirmed the visual improvement of the wrinkles on the volunteers over the 2, 4 and 6 month test period.

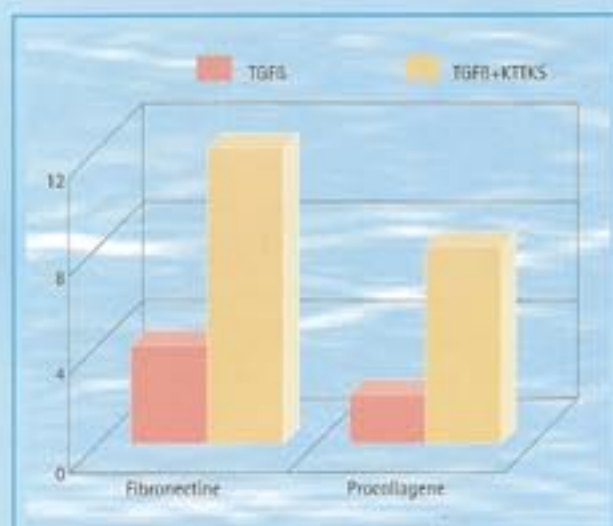
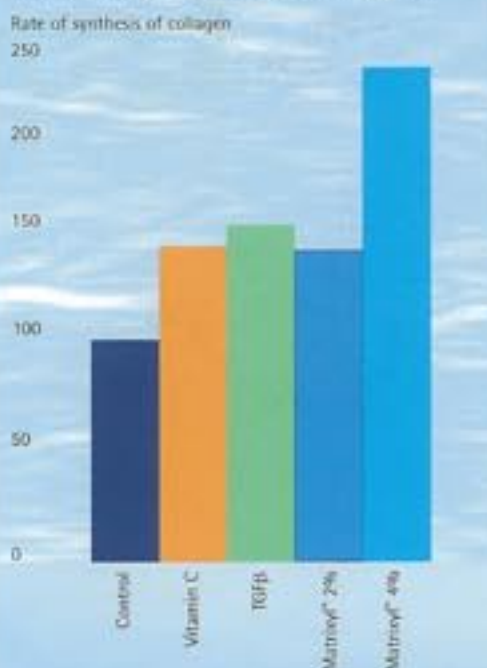
Claim substantiation *in vitro* on human fibroblast culture



+267% of synthesis of glycosaminoglycans with 2% Matrixyl™

Claim substantiation *ex vivo* on human skin biopsies

Stimulation of the synthesis of collagen I



MATRIXYL™

4 months clinical study

Profilometry and image analysis

Function:

MATRIXYL™ constitutes a revolutionary ingredient to treating wrinkles and a remarkable alternative to retinol and vitamin C.

Description:

MATRIXYL™ is a hydroglycolic solution containing 100 ppm of lipopeptide Pal-Lys-Thr-Thr-Lys-Ser.

Properties:

Stimulates the skin fibroblasts in order to reconstitute the extracellular matrix: it leads to the synthesis of collagen I and IV, fibronectine and glycosaminoglycans. This physiological activity, demonstrated *in vitro*, is confirmed by *ex vivo* and overall *in vivo* studies.

Characteristics:

Repairing the **matrix** and the **epidermal-dermal junction** constitutes the mechanism of **wrinkle reduction**. MATRIXYL™ also stimulates wound healing gene expression.

INCI Name:

Glycerin - Water - Butylene Glycol - Carbomer - Polysorbate 20 - Palmitoyl Pentapeptide-3

Applications:

Wrinkle prevention and repair, eye contour, mature skin range of products.

Formulations:

Water soluble

Use levels:

3 - 8%



Two groups of 30 volunteers / Twice-daily application on face and décolleté for 4 months of a cream containing 5% MATRIXYL™ for one group and a placebo for the other / Image analysis by profilometry on Silflo® prints at T0, T2 and T4 months. Biopsies on 12 volunteers.

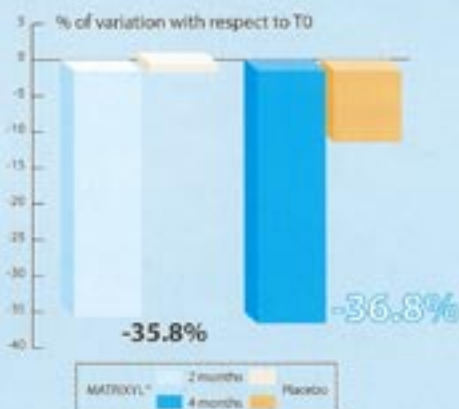
Evolution of the mean depth of the main wrinkle:

A very significant improvement ($p < 0.01$) is seen with MATRIXYL™: 27% at 4 months whereas excipient has no effect.



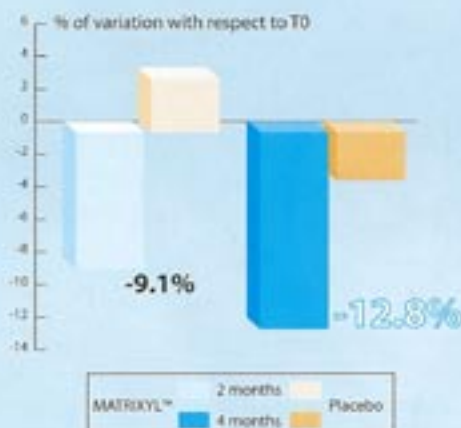
Evolution of the main wrinkle volume:

A very significant improvement ($p < 0.01$) is obtained with MATRIXYL™: -36% at 4 months compared to excipient which shows a slight but not significant decrease.



Evolution of roughness:

A net decrease of roughness is obtained after 4 months treatment with MATRIXYL™: -13% ($p < 0.01$) while the excipient does not vary significantly.



Biopsies:

| ELASTIN | T0 | T4 months | Results |
|---------------------------------------|----|-----------|---|
| Volunteer N°11 treated with MATRIXYL™ | | | Notable increase of density and thickness of fibres |
| Volunteer N°4 treated with Excipient | | | No change |

| COLLAGEN IV | Control | MATRIXYL™ | Excipient |
|------------------------|---------|-----------|-----------|
| Results after 4 months | | | |

Improvement of collagen IV regularity in Dermal - Epidermal Junction with MATRIXYL™

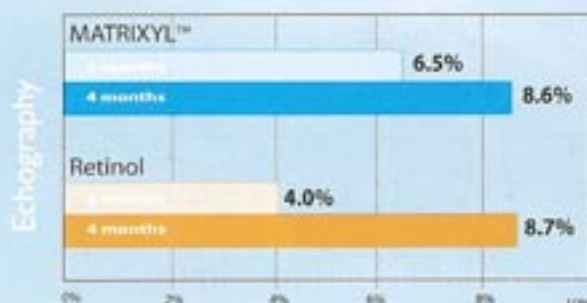
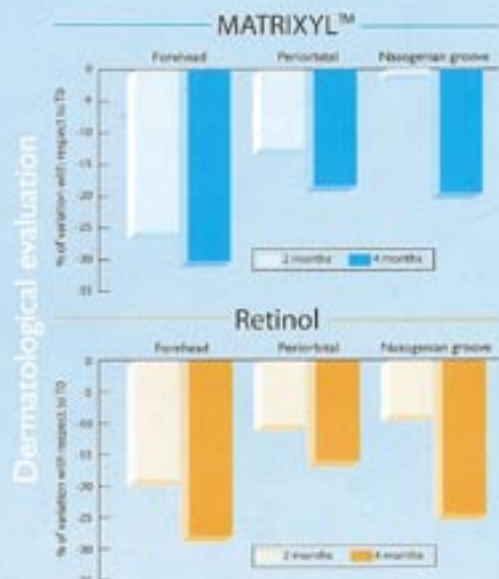
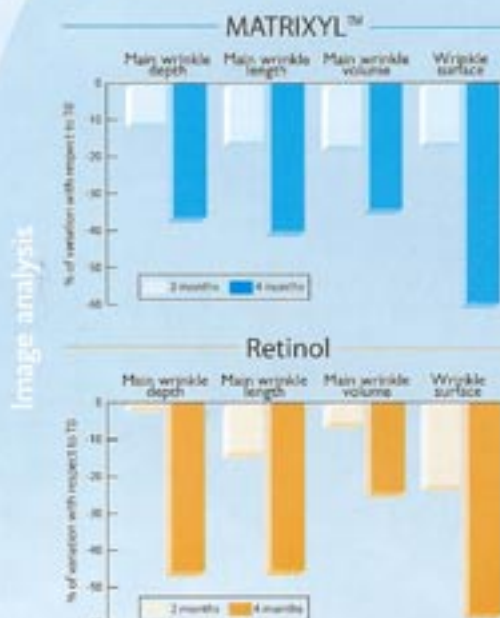
Profilometry and image analysis

16 volunteers / Daily application for two months then twice-daily application for the two following months / Cream containing 3% MATRIXYL™ versus cream containing 0.07% Retinol / Image analysis by profilometry, dermatological evaluation and echography.

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The anti-wrinkle efficacy of MATRIXYL™ is confirmed and acts more rapidly than retinol (and without irritation phenomena). Skin thickness increases by 6.5% in 2 months and 8.6% in 4 months.

Evaluation by the Dermatologist confirms the anti-wrinkle effect, even on the forehead and the perinasal area.

Gene activation

The activity of MATRIXYL™ in comparison to retinol activity is partly explained on the basis of DNA array studies on fibroblasts and reconstituted human epidermis.

| GENE | ACTIVITY |
|---------------------|--------------------------------|
| LOX | collagen cross-linking |
| MMP3 | matrix remodelling |
| 47 kD HSP precursor | CBP1 collagen binding protein |
| HSP 90 | stress protein |
| GSH | synthetase ROS cell protection |

Genes activated by MATRIXYL™ in fibroblasts are consistent with wound healing mechanisms, but do not include the many pro-inflammatory reactions of retinol.



Clinical observations

MATRIXYL™, which peptide belongs to the family of Matrikines (Peptidic fragments, messengers of the natural process of tissue repair), is designed to replace retinol and its esters as an efficient anti-wrinkle active ingredient. It acts through specific mechanisms, without any toxicological danger.

MATRIXYL™ equals and exceeds retinol activity. It can be incorporated in any skin care product, all over the world.

“after 6 months
treatment I can feel my
skin is smoother”

Conclusions

The wide range of tests carried out to study the cosmetic potential of the newly discovered protein fragment, Lys-Thr-Thr-Lys-Ser Micro-collagen™ leads to remarkable coherent results:

the biological activity of the active ingredient, manifest in all test protocols, substantiates our claim that Matrixyl™ with Micro-collagen™ contributes to the appearance of the characteristics of a young, smooth skin.

Its antiwrinkle activity is furthermore markedly superior to the current benchmark, Vitamin C, making it ideal for applications in a variety of areas including:

- anti-ageing products for face and body care
- eye contour preparations
- products for treating mature skin of face, neck and hands

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