THE MESSENGER PEPTIDE FOR DERMAL MATRIX REPAIR:
AN ALTERNATIVE TO RETINOL AND VITAMIN C

Function and Characteristics:
MATRIXYL is a hydroglycolic solution containing 100 ppm of lipopeptide Pal-Lys-Thr-Thr-Lys-Ser. This molecule 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.

Cosmetic interest (properties):
MATRIXYL constitutes a revolutionary ingredient to treating wrinkles and a remarkable alternative to retinol and vitamin C. Repairing the matrix and the epidermal-dermal junction constitutes the mechanism of wrinkle reduction. MATRIXYL also stimulates wound healing gene expression.

Applications:
Products for wrinkle prevention and repair, eye contour care, mature skin range of products.

Recommended use level: 3 to 8%

CTFA / INCI name:
Glycerin - Water (Aqua) - Butylene Glycol - Carbomer - Polysorbate 20 - Palmitoyl Pentapeptide-3

Specifications:
- Appearance: opalescent gel
- Colour: off-white
- Odour: characteristic
- pH: 4.0 – 6.0
- Water content: 20 – 30%
- Density (20°C): 1.140 – 1.160
- Refractive index (25°C): 1.425 – 1.445
- Pal-KTTKS content: > 90 ppm
- Bacteria: < 100 germs/g
- Yeast - Moulds: < 10 germs/g
- Reference: MATRIXV1


CLAIM SUBSTANTIATION

IN VITRO

Summary of the results obtained by KATAYAMA (1993) on peptide Lys-Thr-Thr-Lys-Ser (KTTKS):
- Stimulation of collagen I and III, and fibronectin synthesis: + 320% with 50 µM

Neosynthesis (in these tests, Matrixyl was compared to vitamin C and TGFβ):
- Stimulation of collagen IV synthesis on aged fibroblasts: + 257% with 4% MATRIXYL
- Stimulation of glycosaminoglycan synthesis on fibroblasts: + 267% with 2% MATRIXYL

Molecular biology - Study of gene activation in fibroblasts and in 3D epidermis:

Results: Stimulation of 16 genes specific of skin healing.

Genes | Activity
--- | ---
LOX | collagen cross-linking
MMP3 | matrix tissue remodeling
47 kD HSP precursor | procollagen I linking protein
EGF response factor | growth factor
GSH synthétase | glutathion peroxidase synthesis

EX VIVO

Neosynthesis of collagen on human skin biopsies:
- Stimulation of collagen synthesis:
  - MATRIXYL 2% (2 ppm pal-KTTKS) + 30%
  - MATRIXYL 4% (4 ppm pal-KTTKS) + 117%
  - Vitamin C (1000 ppm) + 42%

Collagen synthesis rate

Control | Vitamin C | 2% Matrixyl | 4% Matrixyl
Profilometry and image analysis - 6-month study:

Against placebo:
25 volunteers / Twice-daily application on half face of a cream containing 3% MATRIXYL versus placebo / Image analysis by profilometry
- Wrinkle depth : -21.6%*
- Roughness : -16.4%*
- Wrinkle volume : -24.4%*
- Main lines density : -46.8%*
- Wrinkles surface : -67.8%*

*significant with regard to t0 (p<0.01)

Before treatment  After treatment

Matrixyl confirms its strong anti-wrinkle efficacy, whereas the cream with vitamin C is inactive

Profilometry and image analysis - 2 and 4-month study versus RETINOL:

Against vitamin C:
10 volunteers / Twice-daily application on half face of a cream containing 3% MATRIXYL versus a commercially available cream containing 5% vitamin C / Image analysis by profilometry
- Wrinkle depth Matrixyl: -21.8%* Vit. C: 1.1%ns
- Roughness Matrixyl: -13.5%** Vit. C: 3.6%ns
- Wrinkle volume Matrixyl: -24.4%* Vit. C: 0.3%ns
- Main lines density Matrixyl: -32.8%** Vit. C: 17.8%ns
- Wrinkles surface Matrixyl: -49.3%** Vit. C: 28.0%ns

* significant with regard to vitamin C (p≤0.07)
** highly significant with regard to vitamin C (p≤0.01)
ns no significant

Before treatment After a 4-month treatment

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.
**In vivo** study in collaboration with Professor REVUZ from Mondor Hospital

Profilingometry and image analysis - 2 and 4-month study versus placebo

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.

### Clinical study:

**Main wrinkle depth**

- Variation with regard to T0 (%)

-24.4%  -26.8%

**Main wrinkle volume**

- Variation with regard to T0 (%)

-35.8%  -36.8%

**Roughness**

- Variation with regard to T0 (%)

-9.1%  -12.8%

* p<0.01 ; ** p<<0.01

### Biopsies:

<table>
<thead>
<tr>
<th>ELASTIN</th>
<th>T0</th>
<th>T4 months</th>
<th>Results</th>
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</thead>
<tbody>
<tr>
<td>MATRIXYL</td>
<td>![image]</td>
<td>![image]</td>
<td>Notable increase of density and thickness of fibres.</td>
</tr>
<tr>
<td>Excipient</td>
<td>![image]</td>
<td>![image]</td>
<td>No change</td>
</tr>
</tbody>
</table>

<table>
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<tr>
<th>COLLAGEN IV</th>
<th>T4 months</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>MATRIXYL</td>
<td>![image]</td>
<td>Regular distribution</td>
</tr>
<tr>
<td>Excipient</td>
<td>![image]</td>
<td>Irregular distribution</td>
</tr>
</tbody>
</table>

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.