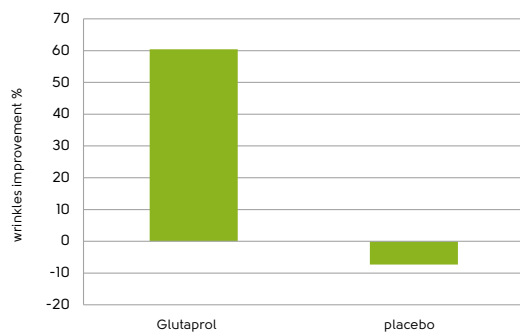


# GLUTAPROL®

Most procollagen products on the market focus on the protection of already synthesized collagen against enzymatic degradation. In aging skin, however, there is a greater degree of synthesis of incomplete collagen, which must be immediately degraded, thus reducing the efficiency of its synthesis (Son et al., 2007). This is combined with the fact that, with age, there is a poorly controllable overall decline in its synthesis (Figiel et al. 2003). The result is wrinkled, drooping skin. Glutaprol is an esterified form of  $\alpha$ -ketoglutarate, which is a natural cofactor in the hydroxylation of proline in the cell. Proline is a key component of collagen fibers and its sufficient hydroxylation is essential for the successful completion of synthesis and the subsequent correct conformational arrangement of the entire collagen fiber.

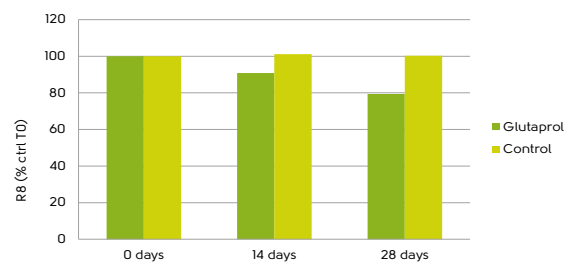
## Wrinkle reduction



Wrinkles reduction after Glutaprol treatment;  $p = 0.015$ , 3D LifeViz measured.

Four weeks' application of cream containing 0.01% Glutaprol in a group of volunteers aged between 28 and 46 years was found to reduce wrinkles by 60%.

## Skin elasticity improvement

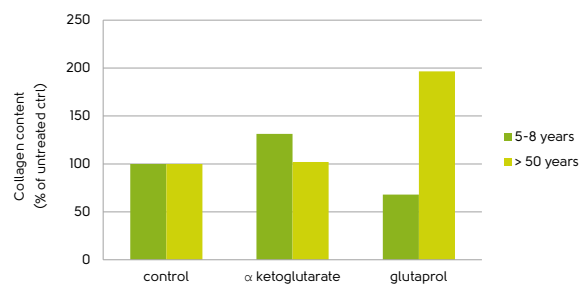


Improvement in the viscoelastic properties of skin: Parameter R8 represented by the viscoelastic coefficient (Ua). The closer the value to zero, the greater the ability of the skin to reconstitute itself after mechanical stress; daily application for four weeks, volunteers aged 28 to 46 years, placebo controlled, 3D LifeViz measured.

Although collagen fibers are mainly responsible for skin strength, their qualitative and quantitative condition is also reflected in viscoelastic parameters. During the *in vivo* study, skin elasticity improved by almost 20% following the application of Glutaprol.

## Mechanism of action

Over time, the cells of aging skin generally lose their viability and synthetic efficiency, manifested by the reduced production of necessary materials. This decrease in efficiency also applies to the hydroxylation of proline during the intracellular phase of collagen synthesis. As a consequence, the old cells produce less collagen, less efficiently. Following the *in vitro* application of Glutaprol, a significant increase in the amount of collagen produced was observed. Since we did not record an adequate increase in mRNA for collagen (data not shown), we assume that Glutaprol has a procollagen effect on the level of support for the hydroxylation of collagen proline. This improves production efficiency, while the rate of synthesis remains unchanged. This hypothesis is supported by the fact that, in young fibroblasts with higher metabolic activity, Glutaprol was not found to have a significant procollagen effect, probably due to the preferential utilization of Glutaprol in the energy metabolism.



The impact of Glutaprol on the collagen content in dermal fibroblasts isolated from biopsies of donors of various ages.  $n \geq 4$ , \*  $p < 0.05$  (0.017) for a comparison of Glutaprol x control (picrosirius red method).

All data were obtained in the relevant *in-vivo* and *in-vitro* measurements and, subject to registration, can be accessed at [www.contipro.com/anti-aging](http://www.contipro.com/anti-aging)

## SPECIFICATION: **Glutaprol**® solution

|                                    |                            |
|------------------------------------|----------------------------|
| Origin                             | chemical processing        |
| Appearance                         | pale yellow, oily solution |
| Hexylesters of alpha-ketoglutarate | present                    |
| Microbial contamination (CFU/ml)   | ≤ 100                      |
| Residual hexan-1-ol (% w/w)        | < 3.0                      |

### SOURCE

- by synthetic processes
- non-GMO used during the manufacturing process
- non-animal materials used during the manufacturing process

### COMPATIBILITY AND PROCESSING

- Glutaprol is recommended for w/o emulsions
- not suitable for aqueous solutions

### SOLUBILITY

- insoluble in water
- soluble in 1,3-butanediol, polyethylene glycol, organic solvents
- soluble in mineral oils

### TOXICOLOGY

- non-irritating
- non-cytotoxic
- non-phototoxic

### Literature:

Fligiel SE, Varani J, Datta SC, Kang S, Fisher GJ, Voorhees JJ. Collagen degradation in aged/photodamaged skin *in vivo* and after exposure to matrix metalloproteinase-1 *in vitro*. *J Invest Dermatol.* 2003;120(5):842-8.

Son ED, Choi GH, Kim H, Lee B, Chang IS, Hwang JS. Alpha-ketoglutarate stimulates procollagen production in cultured human dermal fibroblasts, and decreases UVB-induced wrinkle formation following topical application on the dorsal skin of hairless mice. *Biol Pharm Bull.* 2007; 30(8):1395-9.

