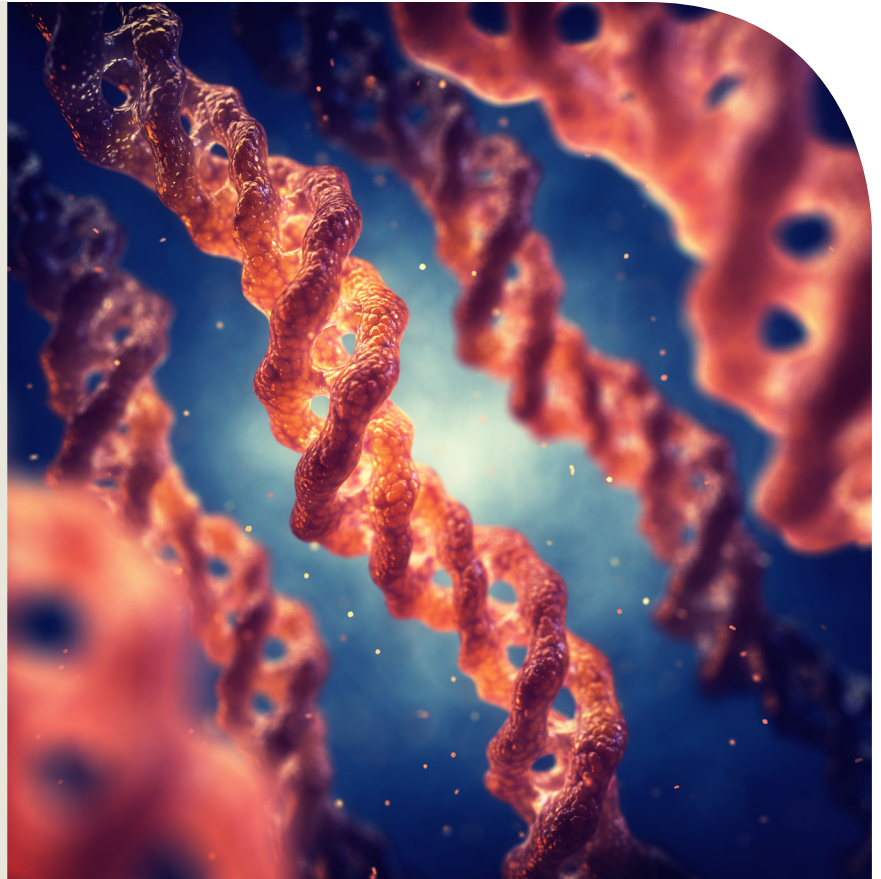




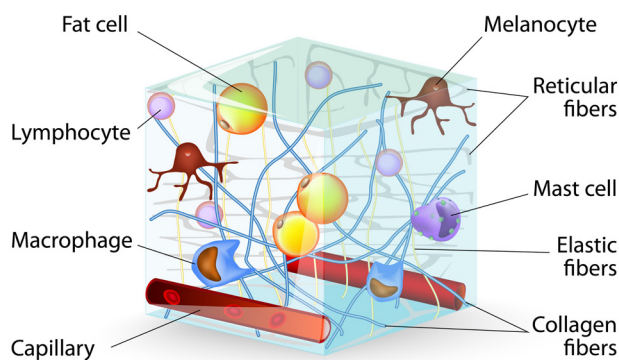
Naticol® and Collagen synthesis

Collagen is the first most abundant protein in the organism. Collagen serves important mechanical functions throughout the body and in particular in the connective tissues. It provides most of the biomechanical properties of the extracellular matrix essential for its functioning. It contributes to the strength, support, shape and elasticity of tissues. However, this collagenous matrix is one main target of destructive processes.



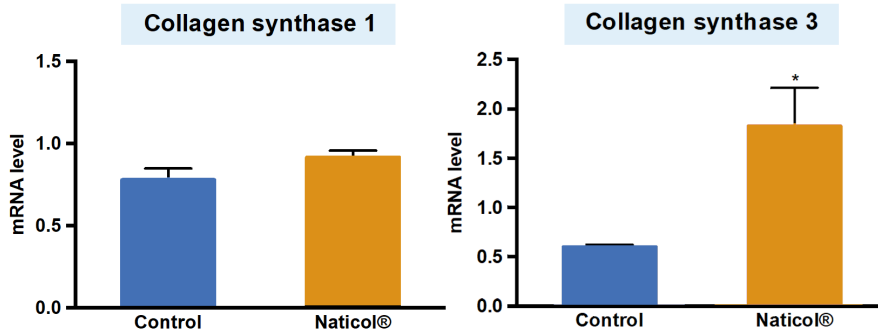
WELL-BEING

CONNECTIVE TISSUES



IN-VITRO ASSESSMENT OF NATICOL® BENEFITS

Human monocyte-derived macrophages (h-MDMs) and keratinocytes (HaCat) were co-cultivated in transwell culture system. The cells were stimulated with LPS (100ng/ml) to induce a pro-inflammatory phenotype and then were treated with Naticol® (1mg/ml). The expression of Collagen Synthase 3 (enzyme involved in collagen production), Metallopeptidase 13 (MMP13 involved in the breakdown of extracellular matrix containing collagen and tissue remodeling), TGF-β and IL-10 (anti-inflammatory and proresolutive cytokines) were evaluated by real-time qPCR.



Figures 1 - Expression of collagen synthase on keratinocytes

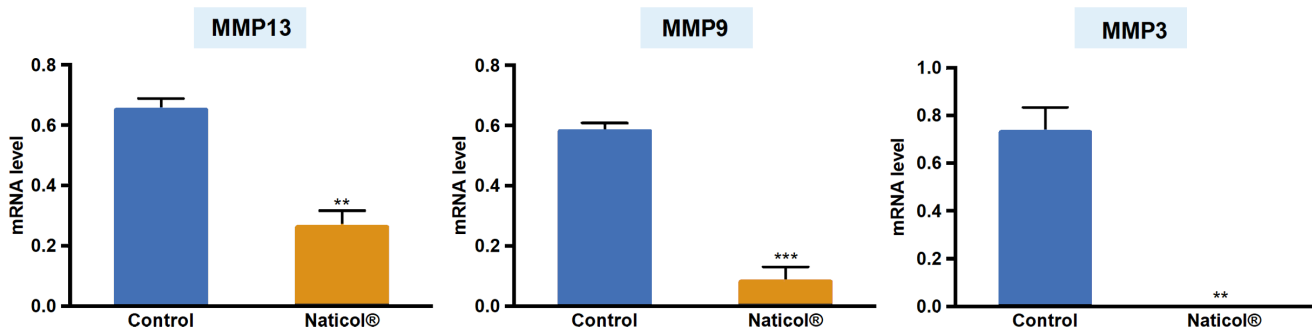


Figure 2 - Expression of metalloproteases on keratinocytes

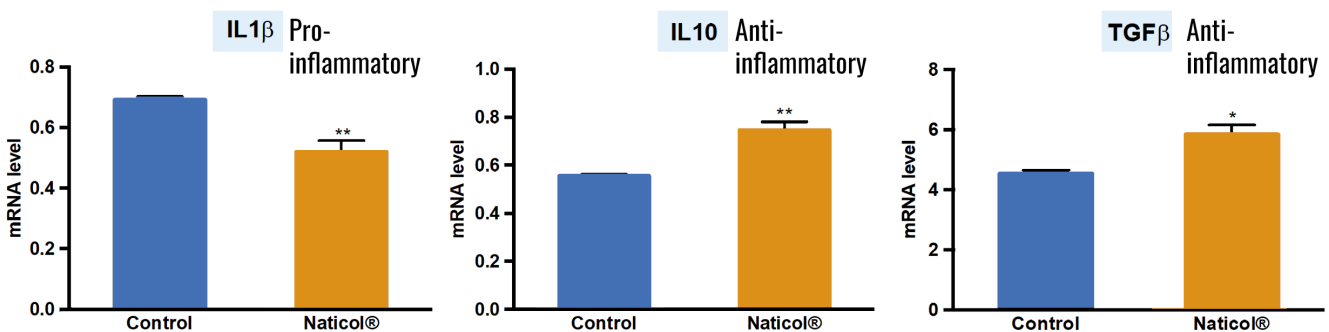


Figure 3 - Expression of cytokines on keratinocytes

Figures 1: Expression of collagen synthase 1 and collagen synthase 3 (keratinocytes) ; **Figures 2:** Expression of MMP13, MMP9 and MMP3 (keratinocytes); **Figures 3:** expression of TGF-β (keratinocytes), IL-10 (keratinocytes) and TGF-β (keratinocytes) * $p < 0,05$; ** $p < 0,01$; *** $p < 0,005$

Figures 1 and 2 show a significant increase of the collagen synthesis with Naticol®. It is due to an increase of the collagen synthase 3 and a decrease of MMP13. An increase in the level of expression of anti-inflammatory and proresolutive cytokines (TGF-β and IL-10) was also observed with Naticol®.

Conclusion

Naticol® presents various competitive advantages. It has demonstrated its anti-inflammatory benefits and its ability to increase collagen synthesis.

These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.