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〈一般論文〉

γ-グルタミルトランスペプチダーゼ（GGT）阻害剤による コラーゲンおよびエラスチン産生能の亢進効果とそのメカニズム

湯浅（小島）明子*, [1]，林　綸子[1]，韓　立友[2]，渡辺文太[3]，平竹　潤[3]，湯浅　勲[1]

A γ-Glutamyl Transpeptidase（GGT）Inhibitor Enhances Collagen and Elastin Synthesis

Akiko KOJIMA-YUASA*, [1], Rinko HAYASHI[1], Liyou HAN[2], Bunta WATANABE[3], Jun HIRATAKE[3], Isao MATSUI-YUASA[1]

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Abstract

A decrease in the quantity and organization of connective tissue is associated with skin aging. Skin connective tissue is composed primarily of fibrillar collagen bundles and elastic fibers. An age-associated reduction in the expression of these dermal connective tissue elements is responsible for skin wrinkling. We have previously reported that a reduction of intracellular glutathione（GSH）levels induces progression of collagen synthesis. In this study, we investigated that the anti-aging effect and the mechanism of action for an inhibitor（GGsTop™）of γ-glutamyl transpeptidase（GGT）, an important enzyme in glutathione（GSH）degradation, using human skin fibroblasts and the HaCat keratinocyte cell line. A treatment of human skin fibroblasts with GGsTop™ induced collagen and elastin synthesis and increased the expression of α-smooth muscle actin（α-SMA）. Additionally, GGsTop™ induced the expression of heat shock protein 47（HSP47）, a collagen-specific molecular chaperone. After 24 hours of treatment, the levels of transforming growth factor-β（TGF-β）secretion were significantly elevated. However, the expression of matrix metalloproteinase-1（MMP-1）was not affected by the treatment of GGsTop™. Cells treated with GGsTop™ also showed an increased production of intracellular reactive oxygen species（ROS）level after 6 h. Conversely, intracellular GSH levels were reduced at 8 h after treatment. Furthermore, GGsTop™ treatment also enhanced the migration of HaCaT keratinocytes. Collectively, these results provide new insights into the cosmetology of GGsTop™ in human skin fibroblasts and keratinocytes and suggest potential applications in the treatment of aging skin.

Key words:　γ-glutamyl transpeptidase（GGT）inhibitor, human skin fibroblasts, HaCaT cells, collagen, elastin.