

The Effect of Glycolic Acid on Human Dermal Fibroblasts: Increased Collagen Synthesis and Inhibition of MMP-2/9

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Alpha hydroxy acid (AHA) includes a group of organic acids found in natural foods such as sugarcane (glycolic acid), milk (lactic acid), apples (malic acid) and oranges (citric acid). Earlier studies demonstrated the effect of AHAs on the skin by diminishing the adhesiveness of the corneal layer and increasing the viable epidermal thickness. Recent data suggest that AHAs have some effects on the dermal component of skin and even affect the aging process of the skin. A previous study revealed increased collagen production by treatment with glycolic acid among AHAs *in vitro*. However, the mechanism of the regulation of collagen production by glycolic acid was unclear. In present study, we tried to demonstrate the effect of glycolic acid on human dermal fibroblasts and to unveil the mechanism of regulation of collagen production by glycolic acid in human dermal fibroblasts: proliferation of fibroblasts and collagen synthesis and degradation by collagenases in fibroblasts. Our results suggested that glycolic acid had no effect on proliferation and cytotoxicity of adult human dermal fibroblasts. However, glycolic acid not only induced the increase of the collagen synthesis in human dermal fibroblasts at lower concentration than 0.1 % but also inhibited MMP-2 activity of human dermal fibroblast in the range between 0.01 and 0.4% and MMP-9 activity of human dermal fibroblast in the range between 0.06 and 0.09%. In summary, our results suggest that glycolic acid may increase wrinkle reduction partially by both increase in collagen synthesis and decrease in collagen degradation.

Recent anti-wrinkle cosmetics tend to contain various kinds of alpha-hydroxy acids (AHAs) as their active ingredients. Clinically it has been known that topical application of some AHAs is effective in treating aged and photoaged skin. The effect of AHAs on aged skin includes increased synthesis of glycosaminoglycans, collagen, and possibly elastic fibers. It is believed that such effects are mediated by the functional activation of fibroblasts. Present study was aimed to define the cell proliferative and cytotoxic effects of glycolic acid among AHAs and demonstrated the effect of glycolic acid on the increased collagen synthesis and the inhibited collagenase activity.

1. Cell culture and materials

Human dermal fibroblasts were derived from adult foreskin by the established primary culture method of MTT Inc.. Glycolic acid was purchased from Dupont and all *trans* retinoic acid and ascorbic acid were from Sigma.

2. MTT assay for cytotoxicity and cell proliferation

3. Determination of collagen synthesis

- PICP (Procollagen type I C-peptide) enzyme immunoassay

: de novo synthesis of collagen

enzymes-linked immunoassay kit (Takara, Japan) as according to the manufacturer's instructions (two-step procedure).

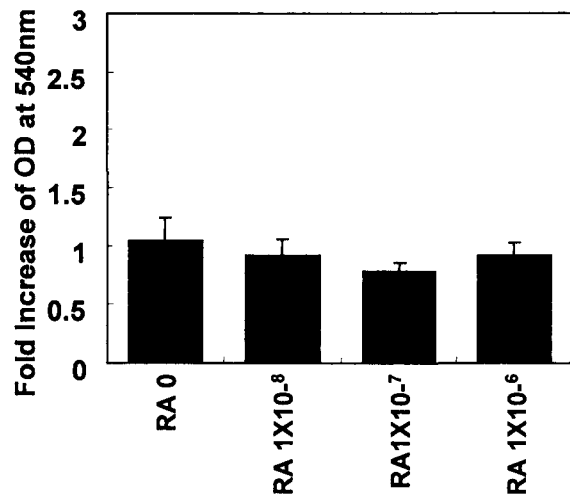
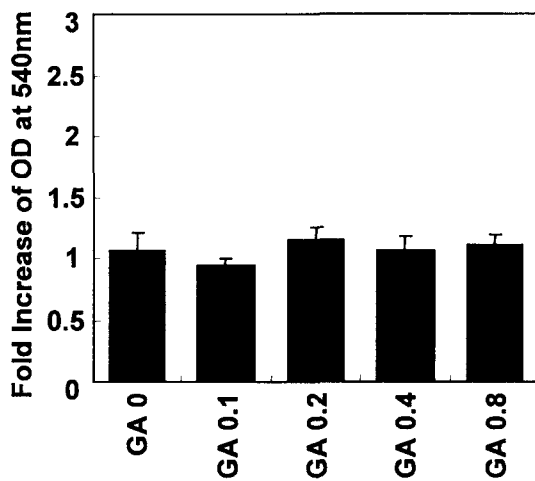
- Sircol collagen assay

: total amount of collagen

4. Zymography assay – collagenase activity

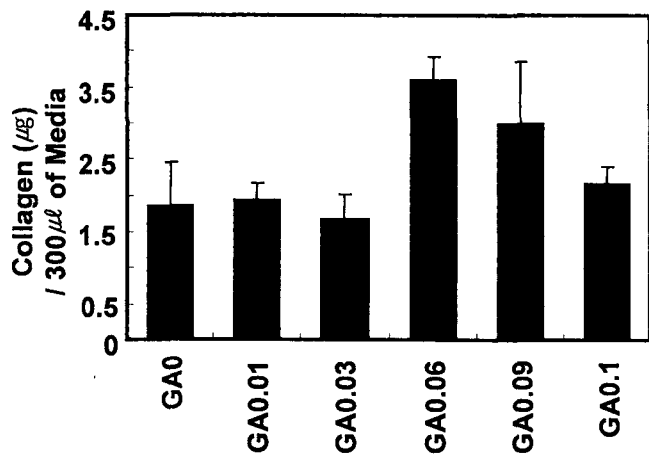
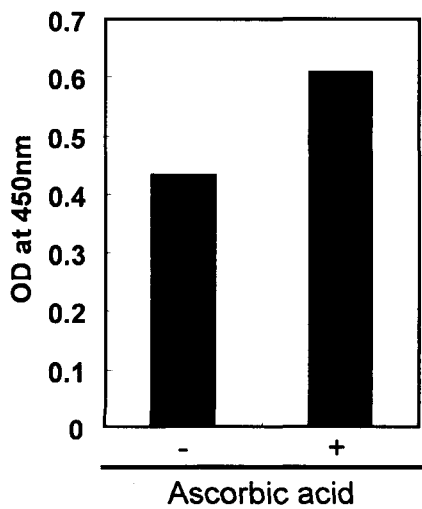
The effect of glycolic acid on the proliferation and cytotoxicity of human dermal fibroblasts

: The glycolic acid had no effect on the proliferation and cytotoxicity of human dermal fibroblasts



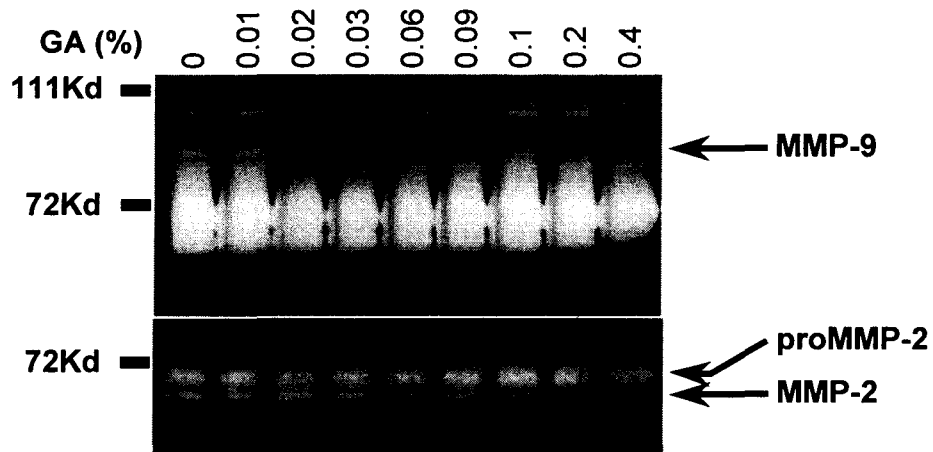
The effect of glycolic acid on collagen synthesis of human dermal fibroblasts

: Glycolic acid induced the increase of collagen synthesis in human dermal fibroblasts in the lower concentration than 0.1 %



The effect of glycolic acid on collagenase activity of human dermal fibroblasts

: Glycolic acid had ability to inhibit collagenase (MMP-2, MMP-9) activity in human dermal fibroblast



Glycolic acid had no effect on proliferation and cytotoxicity of human dermal fibroblasts

Glycolic acid induced the increase of collagen synthesis in human dermal fibroblasts in the lower concentration than 0.1 %

Glycolic acid had ability to inhibit collagenase (MMP-2, MMP-9) activity in human dermal fibroblast

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