Liu Z, J Clin Dermatol Ther 2024, 10: 143
DOI: 10.24966/CDT-8771/100143

HSOA Journal of Clinical Dermatology and Therapy

Commentary

Glutamic-Acid Grafted Hyaluronic Acid Inhibits Inflammatory Factors via Fibroblast and Skin Model Tests

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In the pursuit of more effective cosmetic ingredients for combating skin inflammation, the recent study, Applications presents a novel approach. By conjugating Glutamic Acid (Glu) to low-molecular-weight Hyaluronic Acid (HA), the researchers aimed to leverage the anti-inflammatory properties of both compounds for improved skin health outcomes.

The study describes how excessive inflammation can compromise the skin barrier and lead to issues like aging and various skin diseases [1-3]. Interleukins and tumor necrosis factors, specifically IL-1α, IL-6, and TNF-α, are reported to play pivotal roles in these processes [4-9]. HA, known for its regulatory role on inflammatory factors [10,11], was modified with Glu, an amino acid with reported influence on inflammation [12,13]. This modification aimed to combine the beneficial properties of both substances for enhanced skin care applications.

The synthesis of HA-Glu involved a two-step process adapted from previous works [14,15], leading to the production of HA-Glu with varying degrees of grafting (Figure 1). The anti-inflammatory efficacy was assayed using human dermal fibroblasts and a 3D skin model, comparing the grafted compound against native HA. The results showed that HA-Glu significantly inhibits inflammatory markers IL-1α, IL-6, and TNF-α more effectively than HA alone (Figure 2 for molecular structures, Figure 3 for gene expression comparisons).

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Citation: Liu Z (2024) Glutamic-Acid Grafted Hyaluronic Acid Inhibits Inflammatory Factors via Fibroblast and Skin Model Tests. J Clin Dermatol Ther 10: 143.

Received: September 27, 2024; **Accepted:** October 07, 2024; **Published:** October 14, 2024

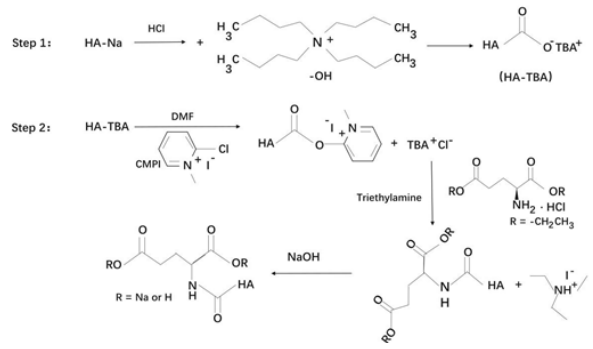

Figure 1: Synthesis reaction of HA-Glu.

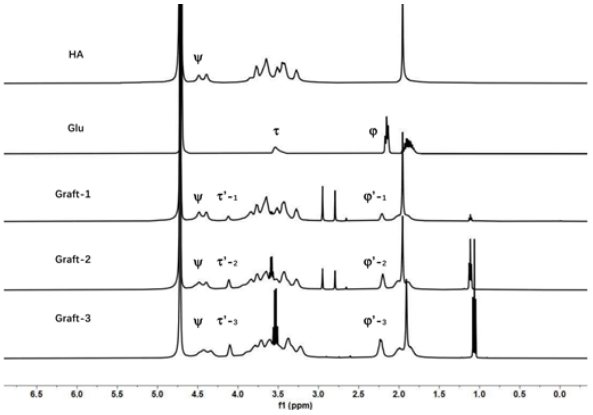

Figure 2: 1H NMR spectra of native HA, L-Glu, and HA-Glus.

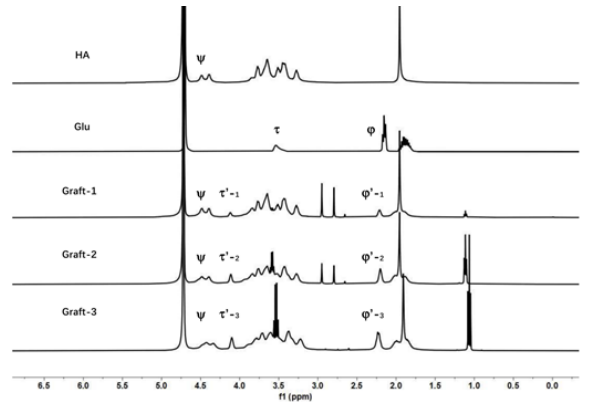

Figure 3: The expression levels of IL-1α, IL-6 and TNF-α in cell tests were detected by qRT-PCR.

Results of IL-1α (A), IL-6 (B), and TNF-α (C) expression in cell tests. (Mean± SD, n = 6). Cell-BC: blank control, Cell-NC: negative control, Cell-PC: 129 ng/mL Dexamethasone sodium phosphate, Cell-1: 150 μg/mL HA, Cell-2: 150 μg/mL Glu, Cell-3:150 μg/mL Graft-1, Cell-4: 150 μg/mL Graft-2, Cell-5: 150 μg/mL Graft-3. **P<0.01 vs Cell-BC; ##P<0.01 vs Cell-NC.

In addition to molecular and cellular assays, the 3D skin model demonstrated the functional benefits of HA-Glu on skin repair. HA-Glu was shown to ameliorate skin damage by enhancing the compactness of the stratum corneum and increasing the thickness of living cell layers (Figure 4 for ELISA results and Figure 5 for skin sample histology) [16-22].

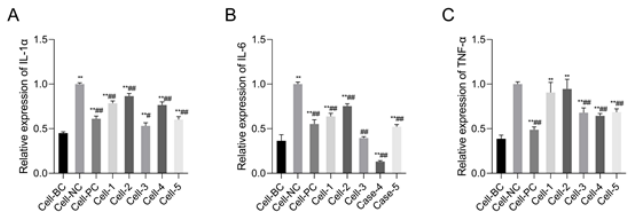

Figure 4: The expression levels of IL-1α, IL-6 and TNF-α in 3D model tests were detected by ELISA.

Results of IL-1α (A), IL-6 (B), and TNF-α (C) expression in 3D model tests. (Mean ± SD, n = 6). Model-BC: blank control, Model-NC: negative control, Model-PC1: 16.19 μg/mL Pirinixic acid, Model-PC2: 100 μg/mL Dexamethasone, Model-1: 500 μg/mL HA, Model-2: 250 μg/mL Graft-1, 250 μg/mL Graft-3. **P<0.01 vs Model-BC; ##P<0.01 vs Model-NC.

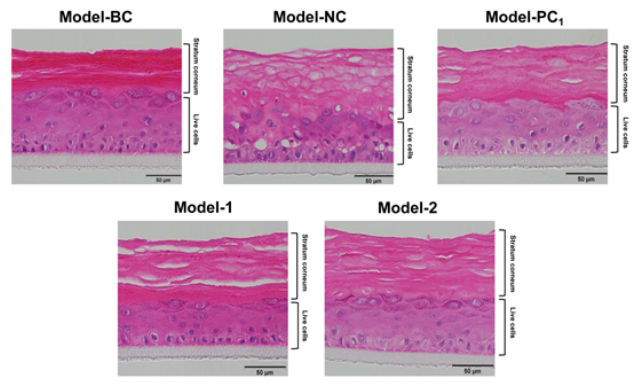

Figure 5: H&E staining results of 3D skin model tests.

(Pink color: cytoplasm of cells; blue-purple color: nuclei) Model-BC: blank control, Model-NC: negative control, Model-PC1: 16.19 μg/mL Pirinixic acid, Model-PC2: 100 μg/mL Dexamethasone, Model-1: 500 μg/mL HA, Model-2: 250 μg/mL Graft-1, 250 μg/mL Graft-3.

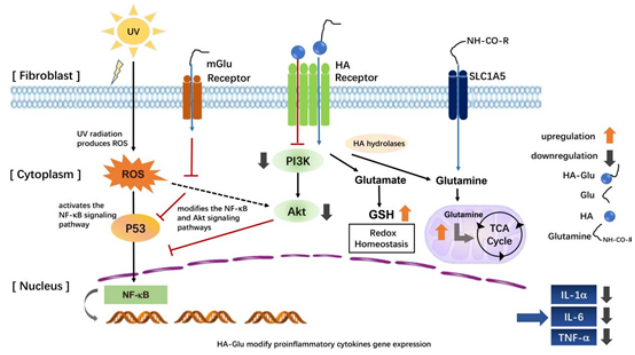

Figure 6: Explanation of the inhibition mechanism of HA-Glu in HDFs.

The work suggests that the synergistic relationship between HA and Glu contributes to the improved outcomes. While HA facilitates Glu's interaction with cells and slows its own degradation, Glu provides additional antioxidant benefits and supports redox balance (Figure 6). The study concludes that HA-Glu holds significant promise for reducing inflammation-induced skin issues and signs of aging, positioning it as an effective ingredient in skin care formulations.

Commentary: This innovative research offers a compelling advancement in cosmetic biochemistry by introducing a grafted molecule that could revolutionize skin care formulations. The meticulous approach to synthesizing and testing the HA-Glu compound underscores the potential of bio-conjugates in enhancing therapeutic benefits. Future studies may explore long-term clinical outcomes and potential side effects to further validate its efficacy and safety for widespread cosmetic use. Additionally, examining the interactions of HA-Glu with other skin components, such as the microbiome, could provide further insights into its holistic impact on skin health.

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