Mandom is the first in the industry to discover that "low molecular weight hyaluronic acid improves rough skin"

Confirmation of its deep penetration into the stratum corneum and the promotion of polymeric hyaluronic acid production

Mandom Corporation (headquarters: Osaka City, President & CEO: Motonobu Nishimura; hereinafter referred to as "Mandom") has discovered that low molecular weight (LMW) hyaluronic acid enhances the recovery time of barrier strength in rough skin. Mandom has proposed that LMW hyaluronic acid deeply penetrates the stratum corneum, acting on cells within the dermis to promote the production of polymeric hyaluronic acid.

The results of this research were presented at the "130th Annual Meeting of the Pharmaceutical Society of Japan," which was held between March 28 and 30.

<Background of Research>

In the body, hyaluronic acid surrounds cells, collagen, and other nutrients, resulting in skin flexibility. Hyaluronic acid also possesses excellent moisture retention capacity as 1 g of hyaluronic acid can hold an estimated 6 liters of water. Furthermore, it is widely used as a moisturizer in cosmetics.

Hyaluronic acid is composed of two repeating sugars, N-acetylglucosamine and glucuronic acid (Figure 1). Polymeric hyaluronic acid contains many of these repeating subunits while low molecular weight hyaluronic acids contains a small number of such repeats.

It has been reported that LMW hyaluronic acid has higher penetrability into the stratum corneum and better sustained moisturizing effect than polymeric hyaluronic acid. Research on its effect when applied to the skin and its impact on hyaluronic acid production have not been reported. Therefore, Mandom has been advancing research aimed to elucidate the effect of LMW hyaluronic acid on the skin.

Owing to these investigations, Mandom has become the first in the industry to discover the improved effect exhibited by LMW hyaluronic acid on rough skin. We propose that LMW hyaluronic acid penetrates deep into the stratum corneum, acts on cells in the dermis and promotes the production of polymeric hyaluronic acid.

Contact

mandom corp.
Public Relations Div.
mail: press@mandom.co.jp
Please contact us in Japanese or English.
URL: https://www.mandom.co.jp/en/

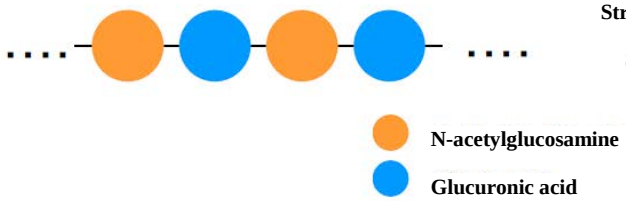

Figure 1. Structure of hyaluronic acid

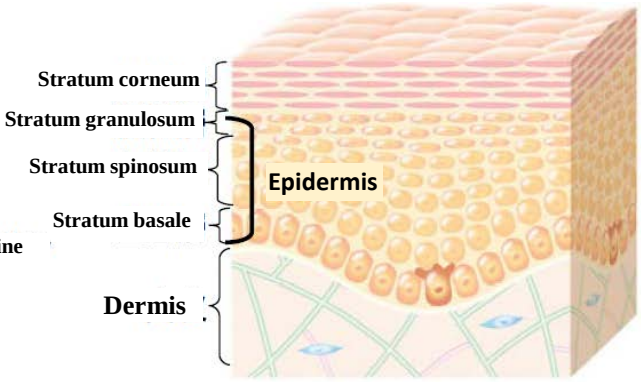

Figure 2. Structure of skin

<Improvement effect of low molecular weight hyaluronic acid on rough skin>

To evaluate moisture barrier strength, we applied LMW hyaluronic acid solution, polymeric hyaluronic acid solution, and water twice per day (morning and night; three days) to the arms of subjects (age range, 20-40+; having provided informed consent) where rough skin (*2) was induced by stripping tape (*1).

In areas where only LMW hyaluronic acid was applied, moisture barrier strength recovered 2-fold compared to areas where water was applied (Figure 3). Therefore, LMW hyaluronic acid contributed to the recovery of moisture barrier strength.

*1 Tape stripping: A method using cellophane tape to remove stratum corneum and reduce barrier strength.

*2 Rough skin: Skin with decreased moisture barrier strength.

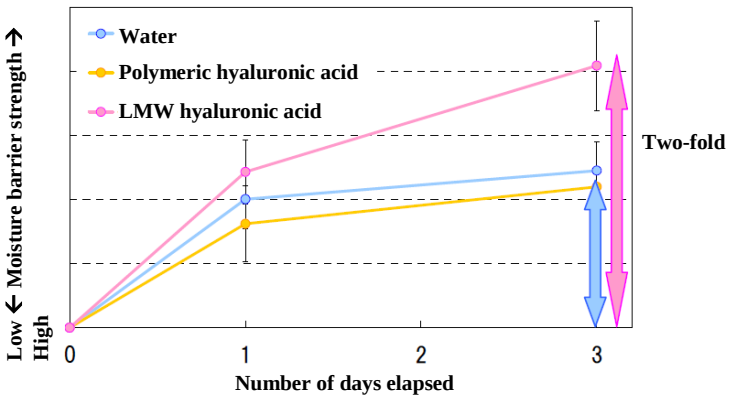

Figure 3. Recovery of barrier function by low molecular weight hyaluronic acid

We performed several experiments to elucidate the mechanism driving the “Improved effect on rough skin” demonstrated by low molecular weight hyaluronic acid.

<Elucidating the mechanism (1): Low molecular weight hyaluronic acid penetrates deep into the stratum corneum>

We performed tape stripping on model skin, induced rough skin, and demonstrated the penetrability of low molecular weight hyaluronic acid. Not only did LMW hyaluronic acid reach the stratum corneum and epidermis, but slight transport to the dermis (Figure 4) was observed. In a similar experiment, polymeric hyaluronic acid did not penetrate the stratum corneum, the uppermost layer of the skin.

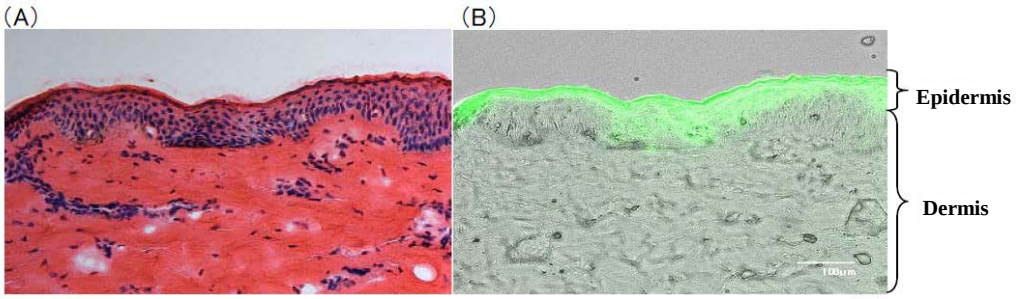

Figure 4. Penetration of LMW hyaluronic acid in the rough skin model

(A) Photo of skin after LMW hyaluronic acid was applied
Sample has been stained to distinguish between epidermis and dermis

(B) Photo visualizing LMW hyaluronic acid
Green area indicates LMW hyaluronic acid.

<Elucidating the mechanism (2): Acting on cells in dermis and promoting hyaluronic acid production>

Fibroblasts present in the dermis are representative of cells that synthesize hyaluronic acid. Addition of LMW hyaluronic acid solution to a culture solution of these fibroblasts increased the gene expression of HAS1, the polymeric hyaluronic acid synthase, and TGF-β1, the controller of HAS1 (Figure 5). Although HAS1, HAS2 and HAS3 are enzymes known to synthesize hyaluronic acid, HAS1 is a known synthesizer of hyaluronic acid.

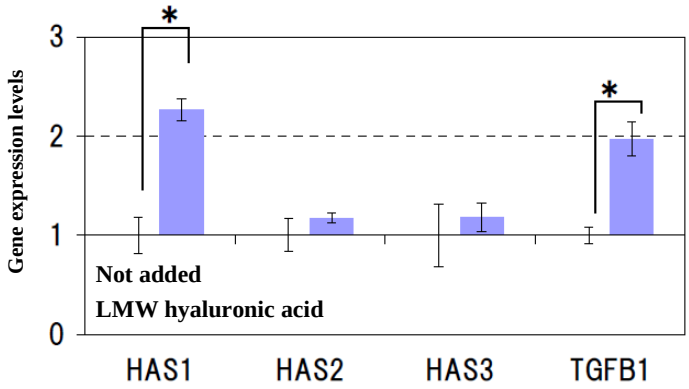

Figure 5. Impact of hyaluronic acid on gene expression

HAS1, HAS2, HAS3: Hyaluronic acid synthases

TGF-β1: A gene that increases HAS1 expression

By adding LMW hyaluronic acid, we confirmed that the production of polymeric hyaluronic acid increases in fibroblasts. Therefore, we now understand that the addition of LMW hyaluronic acid promotes the production of hyaluronic acid with higher molecular weight (Figure 6).

These results suggest that LMW hyaluronic acid increases the activity of hyaluronic acid synthases and enhances the production of polymeric hyaluronic acid.

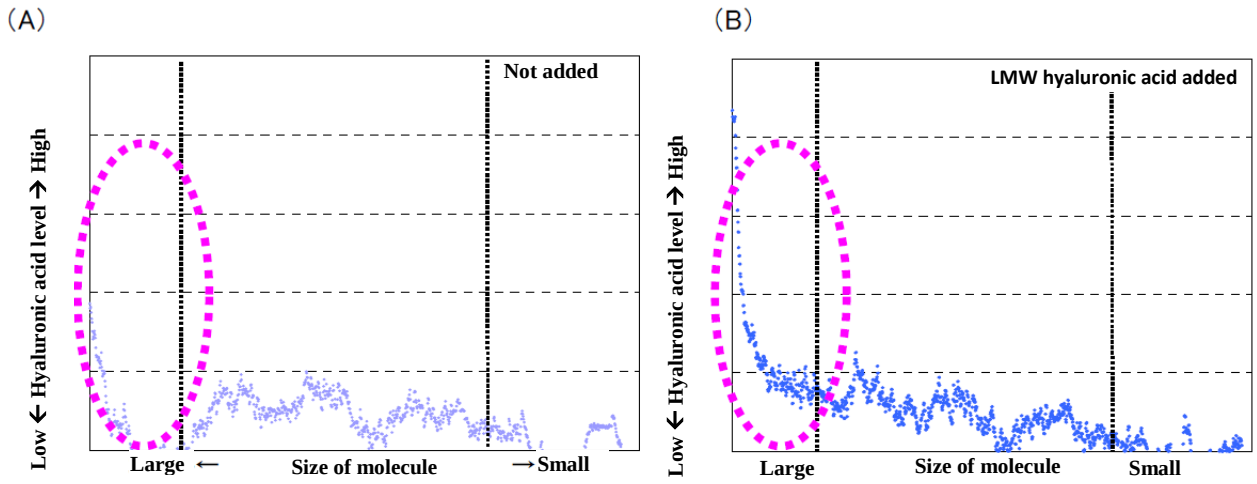

Figure 6. Promotion of polymeric hyaluronic acid production by LMW hyaluronic acid

(A) Production level and molecular weight of hyaluronic added with LMW HA addition

(B) Production level and molecular weight of hyaluronic acid with LMW HA addition

※ indicates the level of polymeric hyaluronic acid production; an increase was observed with LMW hyaluronic acid addition.

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The above results suggest that LMW hyaluronic acid contributes to the recovery of barrier function in the skin by penetrating the rough skin and promoting the synthesis of polymeric hyaluronic acid (i.e., LMW hyaluronic acid is "Hyaluronic acid that increases the hyaluronic acid content in the skin", which penetrates rough skin and produces polymeric hyaluronic acid in the skin). We therefore expect LMW hyaluronic acid to increase polymeric hyaluronic acid in the skin in an effort to recover barrier function, and elevate the moisture retention capacity of the skin, to provide subsequent flexibility in the skin.

Mandom will continue its strive to create products to achieve "ideal skin" that will allow people to feel comfortable; this will be performed by studying the skin's ingredients to achieve better skin.

We also plan to apply the findings of this research to our company's cosmetic products for women, namely the warm-moisturizing skincare series, Barrier Repair.

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