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A Cause of Hypersensitivity in Sensitive Skin is Revealed Improving Epidermal Tight Junctions Decreases Discomfort

Kao Corporation's Skin Care Research Laboratory has demonstrated, under the supervision of Professor Kenji Kabashima of the Department of Dermatology, Graduate School of Medicine, Kyoto University, that, compared to healthy skin, sensitive skin that is prone to discomfort contains more nerve fibers extending deep into the stratum corneum (Figure 1), suggesting that this could be led by dysfunction of the epidermal tight junctions, which are part of the skin's barrier system.

Kao has also discovered that γ -amino- β -hydroxybutyric acid enhances the function of epidermal tight junctions in cultured keratinocytes, and has shown that continuous use, for eight weeks, of a prototype formulation containing γ -amino- β -hydroxybutyric acid decreased characteristic tingling and burning discomfort in sensitive skin.

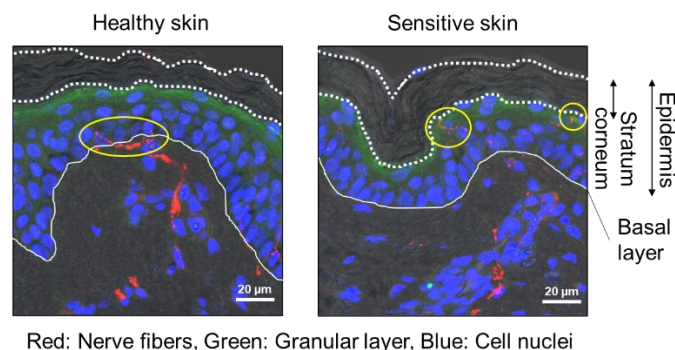


Figure 1. Comparison of nerve fiber distribution in healthy skin and sensitive skin

The results of this research were presented at the 50th Convention of the Japanese Cosmetic Science Society in Tokyo, Japan (July 4–5, 2025), and received the Convention President's Award.

Background

Sensitive skin refers to skin that is highly sensitive and prone to uncomfortable sensations such as pain, itching and tingling in response to stimuli that would not normally trigger a reaction. Kao has for many years been researching skin that, despite the absence of skin disease, is highly sensitive to irritation. Decreased barrier function in the stratum corneum is known to be a factor in sensitive skin, and Kao has been focusing on and elucidating the role of ceramides, which are major structural components of intercellular lipids in the stratum

corneum^{1*}.

The activation of neural activity is also thought to be a factor in sensitive skin, but there was insufficient progress in this field of investigation, and the detailed mechanism by which the uncomfortable sensations arise remained unclear. Kao therefore conducted new investigations focusing on nerve fibers within the epidermis.

*1 “[Sensitive skin with a tendency of decreased skin barrier function has a similar ceramide profile to skin with atopic dermatitis](#),” February 28, 2023 Kao news release (in Japanese).

Sensitive skin contains a greater number of intraepidermal nerve fibers that extend deep into the stratum corneum

The granular layer of the epidermis contains structures known as tight junctions, whose function is to keep neighboring cells in very close contact with each other in order to prevent invasion of foreign substances and evaporation of moisture. Another role of tight junctions is to keep nerve fibers to the inner side of the tight junctions (Figure 2), and it has been reported that in atopic dermatitis, weakening of the tight junctions allows nerve fibers to extend to just below the stratum corneum where they can cause discomfort such as itching.

In order to investigate the relationship between intraepidermal nerve fibers and hypersensitivity, which is a characteristic of sensitive skin, Kao researchers divided a group of Japanese women in their 20s to 50s into a sensitive skin group and a healthy skin group*², and compared the distribution of cutaneous nerve fibers in the skin on the inner sides of their upper arms (Figure 1). It is known that nerve fibers are usually distributed from the basal layer to the granular layer of the epidermis, and the research team has found that in sensitive skin, a significantly higher number of nerve fibers extend deep into the stratum corneum (Figure 3).

*2 Sensitive skin group: lactic acid irritation score (which indicates sensitivity to irritants) of 1.5 or higher (N=3), Healthy skin group: no awareness of sensitive skin, score of 0 (N=3)

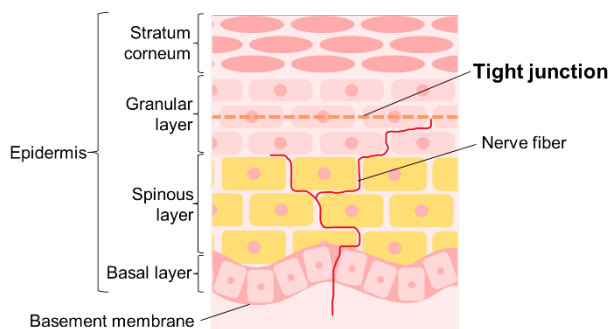


Figure 2. Diagram showing the intraepidermal nerve fiber distribution in healthy skin

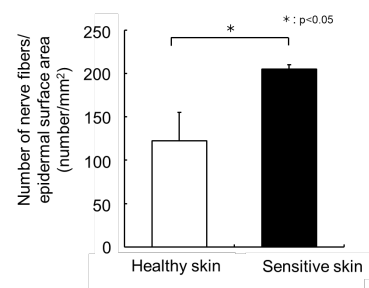


Figure 3. Comparison of the number of nerve fibers reaching to just below the stratum corneum

Sensitive skin tissue exhibits decreased gene expression of claudin-3, a structural component of epidermal tight junctions

In order to investigate the mechanism by which nerve fibers extend deep into the stratum corneum in sensitive skin, the gene expression in skin tissue was comprehensively analyzed. The results revealed that gene expression of claudin-3, which is known to be a structural component of tight junctions, was significantly lower in the sensitive skin group than in the healthy skin group.

Then, in order to investigate whether decreased claudin-3 affects epidermal tight junction function, the

transepithelial electrical resistance (TEER) value, a known indicator of barrier function, was evaluated in normal human epidermal keratinocytes wherein claudin-3 activity had been selectively weakened using genetic engineering techniques. The TEER values were significantly decreased, which shows that claudin-3 contributes to tight junction function.

This suggests that discomfort in sensitive skin is triggered by increased invasion of nerve fibers deep into the stratum corneum, presumably due to decreased epidermal tight junction function with suppressed claudin-3 expression.

The search for cosmetic materials that enhance the function of epidermal tight junctions

Kao searched for cosmetic materials that enhance the function of epidermal tight junctions, with the aim of suppressing excessive extension of nerve fibers. On adding various materials to normal human epidermal keratinocytes and comparing claudin-3 expression, it was found that γ -amino- β -hydroxybutyric acid, an amino acid devivative, (Figure 4) affords significant, dose-dependent increases in claudin-3 expression and TEER values.

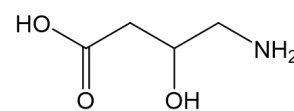


Figure 4. γ -amino- β -hydroxybutyric acid

Also, in an eight-week clinical study in 40 women in their 20s to 40s who were aware of having sensitive skin and had high sensitivity to irritation^{*3}, the subjects were divided into a group of 20 subjects who used a prototype formulation containing γ -amino- β -hydroxybutyric acid, and a group of 20 subjects who used a placebo formulation that contained no γ -amino- β -hydroxybutyric acid. After continuous use for eight weeks, the minimum electrical current perceived as irritation (current perception threshold or CPT) was significantly higher in the prototype formulation group than in the placebo formulation group (Figure 5). Also, a survey conducted after completion of the continuous use study revealed that the proportion of subjects who perceived a decrease in their discomfort such as tingling and burning sensations in daily life was significantly higher in the prototype formulation group than in the placebo formulation group (Figure 6).

^{*3} Those with a 250 Hz current perception threshold (CPT) of 10 or less, using a Neurometer (particularly sensitive to tingling and burning sensations)

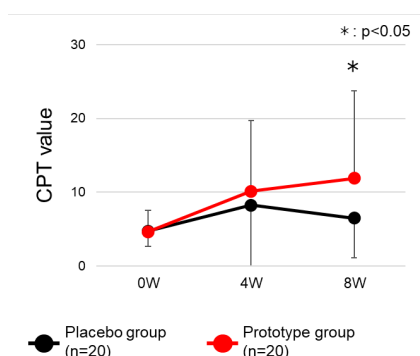


Figure 5. Variation in CPT value on continuous use of formulation

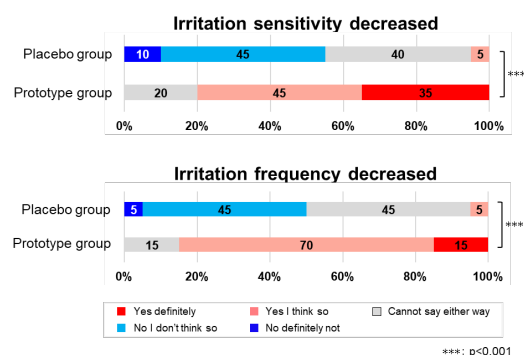


Figure 6. Variation in perceived skin discomfort in daily life

Summary

Kao has revealed that in sensitive skin, the distribution of nerve fibers within the epidermis is altered, and one

reason for the sensitivity to irritation could be the extension of nerve fibers deep into the stratum corneum. Decreased claudin-3 expression is thought to contribute to the changes in the barrier function of epidermal tight junctions.

Also, Kao searched for cosmetic materials that enhance the function of tight junctions, and showed that continuous use of a formulation containing γ -amino- β -hydroxybutyric acid decreased characteristic tingling and burning sensations in sensitive skin.

Kao will continue its research into the structure and function of the skin in order to advance the fundamental understanding of sensitive skin, with the aim of developing skin care technologies that will improve consumers' quality of life.

About Kao

Kao, a Japan-based manufacturer of personal care and household products, cosmetics, and specialty chemicals creates high-value-added products and services that provide care and enrichment for the life of all people and the planet. Through its brands such as *Attack* laundry detergent, *Bioré* and *Jergens* skin care products, *Laurier* sanitary products, *Curél*, *SENSAI*, and *MOLTON BROWN* cosmetics, and *Oribe* hair care products, Kao is part of the everyday lives of people across Asia, the Americas, Europe, the Middle East, and Africa. Combined with its chemical business, which contributes to a wide range of industries, Kao generates about 1,630 billion yen in annual sales. Kao employs about 32,600 people worldwide and has more than 130 years of history in innovation. As an enterprise that provides products people use on a daily basis, the Kao Group takes responsibility to actively reduce the environmental footprint of its products throughout the product lifecycle. This is laid out in Kao's ESG strategy, the Kirei Lifestyle Plan, which launched in 2019.

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