

Press Release

Research and Development

Shiseido Develops Next-Generation Microneedles That Deliver Overwhelming Skin Improvement Effects Safely And At Aesthetic Medicine Levels

Unique Bi-Functional Structure for "Injecting" and "Pressing" to Simultaneously Approach Superficial and Deeper Layers of Skin

Shiseido has developed next-generation microneedles^{*1} (Figure 1) having a unique structure^{*2} that achieve both safety and high efficacy aesthetic medicine quality effectiveness, and can be used daily. This is a new approach featuring two functions, "injecting" and "pressing," allowing the injection of active ingredients into the superficial layer of the skin (the epidermis including the stratum corneum) without damaging the skin, while simultaneously providing stimulation via pressing force to the deeper parts of the skin (below the dermis). This leads to changes in the expression of gene clusters related to immunity, blood vessels, and the extracellular matrix^{*3} including collagen. It was revealed that these changes comprehensively activate the epidermis, dermis, and blood vessels and improve complex skin concerns such as sagging, barrier function, and wrinkles. With this technology, an ideal natural skin beauty can be easily and safely obtained as an extension of daily living. Going forward, Shiseido will continue to strive to create unprecedented new values and lifestyles. The results of this study were partly presented at the 34th IFSCC^{*4} Congress 2024 Brazil Iguazu Falls.

^{*1} Micro-scale ultra-fine needles. The use of microneedles has been promoted in the cosmetic and medical fields as a method to make tiny holes in the stratum corneum and thereby facilitate the intradermal delivery of drugs and cellular activation.

^{*2} Patent pending: WO2022071339A1, WO2023190584A1

^{*3} A complex insoluble macromolecule aggregate consisting of proteins and carbohydrates having a network structure in a gel-like form present in the intercellular spaces of living tissues.

^{*4} IFSCC: The International Federation of Societies of Cosmetic Chemists

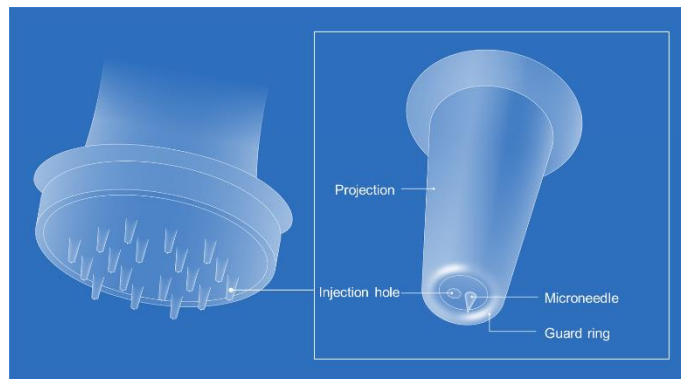


Figure 1. Next-generation microneedles having a unique structure (for illustrative purpose)

Next-generation microneedles equipped with mechanisms of not only "puncturing" but also "pressing" the skin, developed to solve conventional problems

In recent years, cosmetic medicine has become common as a way of realizing ideal skin, and there is a growing expectation for cosmetics to also be highly effective to that end. Microneedles, popularly used in cosmetic medical procedures, make tiny holes in the skin, which is regarded as helping increase the penetration of the active ingredients while also inducing a "wound healing" reaction, allowing the structure deep inside the skin to rebuild and thereby produce high efficacy. On the other hand, there is also an invasive aspect such as bleeding caused by the procedure, so the burden and anxiety when undergoing the procedure have been issues. Shiseido therefore has come up with the idea of realizing simultaneously both high effectiveness and non-invasiveness, paradoxical factors, by adding the new function of "pressing" to the conventional "puncturing" function (Figure 2). Moreover, to solve problems such as limited types and amounts of active ingredients that can be loaded, the safety of the needle material, and the risk of the needles broken, a unique injection mechanism was developed. These new care approaches of "injecting" and "pressing" have been driving the company's research forward, breaking away from conventional thinking.

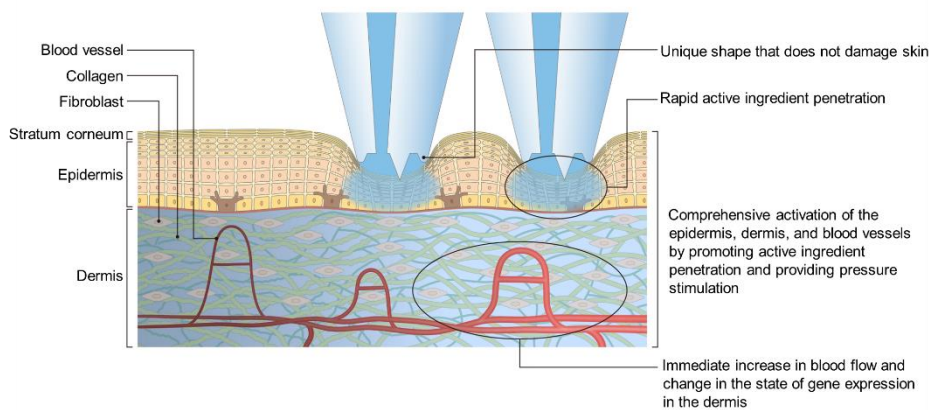


Figure 2. Mechanism of action of next-generation microneedles (for illustrative purpose)

New needle shape for achieving rapid active ingredient penetration

As a result of examining various shapes of microneedles, Shiseido identified shape parameters that allowed for precise penetration of only the superficial layers of the skin while efficiently providing pressure stimulation to the deeper layers, thereby developing a next-generation microneedle with an optimized shape. The microneedles developed through this research are capable of injecting active ingredients into the skin, and the results of evaluation of drug penetration revealed that there was a significant improvement in the amount of penetration of water-soluble drugs such as niacinamide, which were rapidly delivered to deeper parts of the skin (Figure 3).

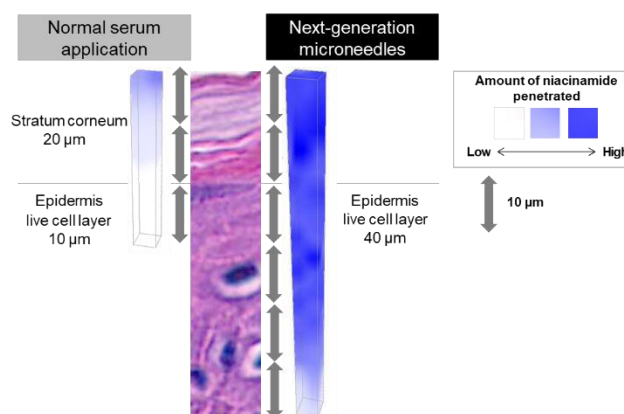


Figure 3. Next-generation microneedles allow niacinamide to be delivered quickly to deeper parts of the skin

Pressing alters the expression of gene clusters related to immunity, blood vessels, and the extracellular matrix, including collagen

The "pressing" effect of next-generation microneedles has been shown to provide compressive stimulation to the deeper layers of the skin, instantly promoting blood flow. Additionally, using these microneedles every other day for seven days stimulates the deeper skin layers, leading to changes in the expression of gene clusters related to immunity, blood vessels, and the extracellular matrix including collagen. These results suggest that these microneedles have the potential for skin improvement without causing damage (Figure 4).

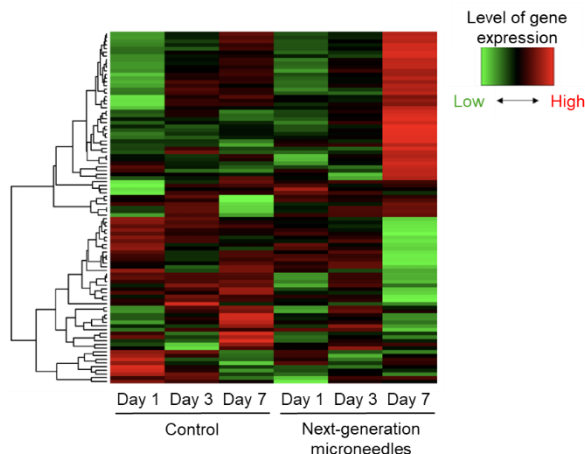


Figure 4. The pressing effect of next-generation microneedles comprehensively altered the expression of gene clusters in the deeper layers of the skin (dermis)

Improvement in complex skin concerns such as sagging, barrier function, wrinkles, and transparency with niacinamide

Shiseido conducted a continuous use study of the next-generation microneedles with niacinamide. The results showed that wrinkles and transparency were improved in a shorter period compared to normal application. In addition, the evaluation of changes in the volume of the lower half of the face revealed a significant decrease in the lower face volume two weeks after the use of the next-generation microneedles (Figure 5). We also confirmed a significant improvement in sagging grade, and that after eight weeks, the nasolabial folds became shallower and shorter (Figure 6). More so, when we evaluated transepidermal water loss (TEWL), it became clear that the next-generation microneedles do not cause destruction of the barrier function, but rather improves it.

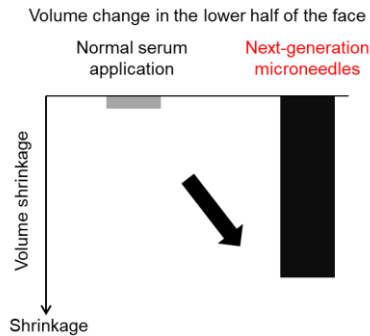


Figure 5. Next-generation microneedles significantly decreased the volume after two weeks



Figure 6. Next-generation microneedles changed the appearance of the nasolabial folds to be shallower and shorter after eight weeks

About Shiseido's R&D strategy:

This study was conducted under "Skin Beauty INNOVATION," one of the three pillars of Shiseido's R&D strategy, with the aim of realizing benefits that go beyond what traditional thinking offer, bringing about overwhelming skin improvement effects and immediate results at aesthetic medicine levels, safely and securely.

- Integrated Report 2023 (Beauty Innovation)
<https://corp.shiseido.com/report/en/2023/message/cmio/>
- Keywords
Skin Beauty INNOVATION, next-generation microneedles

Reference:

Researchers' Challenges

■R&D Philosophy "DYNAMIC HARMONY" approach

This study has been carried out using the Inside/Outside approach of Shiseido's unique R&D philosophy, "DYNAMIC HARMONY." the company's goal was to bring about skin benefits that go beyond what conventional cosmetics offer by utilizing the skin's latent power, working on the skin in a complex manner from inside and outside.

■Achieving both high effectiveness and safety at near-cosmetic medicine levels
Shiseido conducts research to meet the needs of customers with the expectation for cosmetics to also be highly effective. However, effectiveness and safety are paradoxical factors. So how can items with an effectiveness that almost parallels that of cosmetic medicine, which can also be used safely on a daily basis? After careful consideration, we began its researching for new microneedles.

Researchers with different expertise have teamed up to realize methods and functions to approach the deep layers of the skin while protecting it and to establish new experimental methods for elucidating mechanisms and identifying containers that anyone can easily use. It took nearly six years to realize this technology through repeated trial and error. Shiseido believes it is a revolutionary technology that combines functionality and safety at an unprecedented level.

Next-generation microneedles represent a highly expansive technology that enables a wide variety of active ingredients and formulation technologies to be combined freely. The company will continue to advance its research so that it can deliver reliable effects based on science to its customers safely and securely.



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What is research and development (R&D) philosophy "DYNAMIC HARMONY"

- Shiseido Formulates its Unique R&D Philosophy "DYNAMIC HARMONY" (2021)

<https://corp.shiseido.com/en/news/detail.html?n=00000000003252>

- The DYNAMIC HARMONY special website

<https://corp.shiseido.com/en/rd/dynamicharmony/>