Press Release

Research and Development

Shiseido enhances functionality and safety of cosmetic products by visualizing penetration and distribution of active ingredients in the skin with cell-level resolution

Information on the route of penetration of cosmetics and quasi-drug ingredients and the state of delivery to target cells can be acquired, with possible application to formulation

Shiseido, through joint research with Toray Research Center, Inc., developed an innovative analytical technology to observe the distribution of cosmetics and quasi-drug ingredients that have penetrated into the skin with cell-level resolution. Vivid visualization of ingredients penetrating into the inner layers of the skin was made possible by the ultra-high resolution element imaging technology (NanoSIMS) of Toray Research Center, Inc., combined with the human skin observation technology, which is Shiseido's forte. The developed technology will enable the acquisition of valuable information that has previously been considered unobtainable, such as the route of penetration of cosmetics and quasi-drug ingredients inside the stratum corneum and the state of delivery to target cells, thereby accelerating the development of products with higher functionality and safety.

The results of this study were partly presented at the 33rd IFSCC[*1] Congress in Barcelona (Sep. 4-7 2023). (Figure 1)

*1. IFSCC: The International Federation of Societies of Cosmetic Chemists

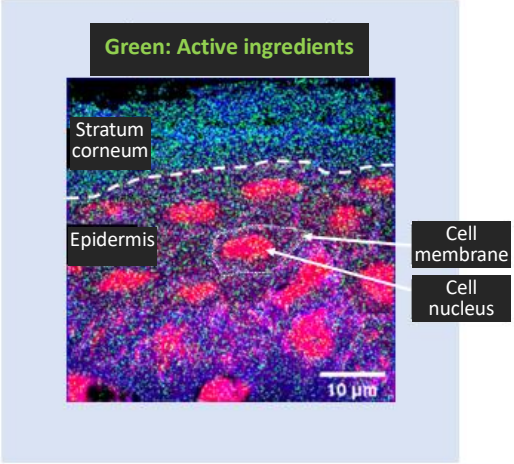

Figure 1. Example of observation by the developed analytical technology: the image shows how active ingredients are penetrating inside the stratum corneum, cell membrane, and cell nucleus

Importance of evaluation of the degree of penetration of ingredients inside the skin and the evaluation method

Evaluating the degree of penetration of active ingredients inside the skin will greatly contribute to the acceleration of product development that combines functionality and safety. In order to evaluate the degree of penetration of ingredients, a method to measure the amount of ingredients extracted directly from the skin after application to the skin using LC/MS[*2] has been used in combination with mass spectrometry imaging techniques to visualize the distribution of ingredients in skin tissue. However, the conventional mass spectrometry imaging techniques lacked sufficient resolution to visualize the distribution of ingredients in extremely small spaces at the cellular level, making it technically difficult to gain a detailed understanding of the route of penetration inside the stratum corneum and the delivery of ingredients to target cells, which are of most interest. In this research, Shiseido

aimed to develop a higher resolution imaging technology with a view to acquiring detailed information, including the route of penetration of ingredients and the state of delivery to target cells, and applying it to formulation that takes into account both functionality and safety.

*2. Analytical technology that combines high performance liquid chromatography (LC) and mass spectrometry (MS)

Technology for visualizing the penetration and distribution of ingredients with cell-level resolution

In this study, we focused on the ultra-high resolution element imaging technology (NanoSIMS) (Figure 2), which has mainly been used for the analysis of trace impurities in industrial materials such as semiconductors. Shiseido, in collaboration with Toray Research Center, Inc. through 3 years of research, has developed an analytical technology*3 for detailed observation of human skin using NanoSIMS, and succeeded in visualizing organelles such as the nucleus with a resolution on the order of nanometers*4, allowing for observation of how ingredients penetrate into the skin (Figure 1).

*3. Patent application has been filed for the invented analytical technology: Patent Application No. 2023-142220

*4. 10^{-9}m

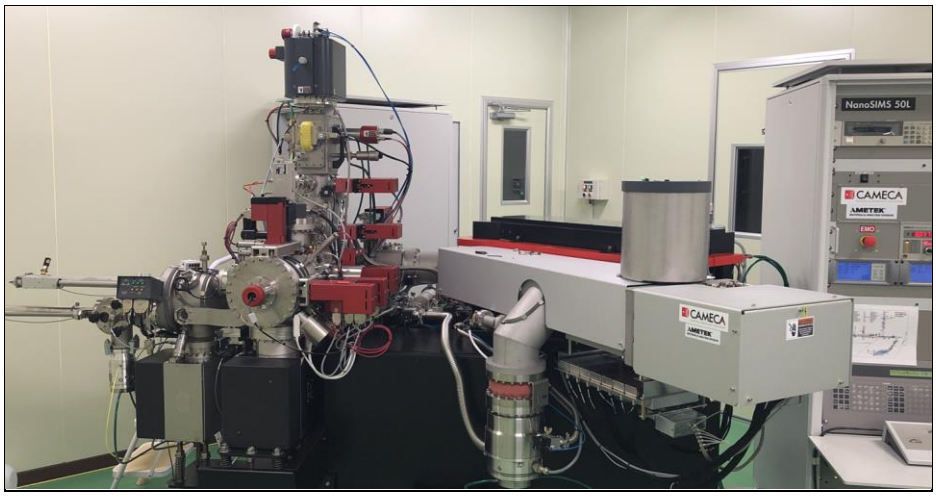

Figure 2: NanoSIMS instrument used in parallel for the development of present analytical technology (NanoSIMS 50L, Cameca, France)

(At the shared facility of Advanced Research Infrastructure for Materials and Nanotechnology in Japan)

Future prospects

With the spread of aesthetic medicine, the levels of functionality and safety demanded by consumers for cosmetics and quasi-drugs are becoming higher every day. By utilizing the analytical technology developed in this study, Shiseido will advance the development of products with higher functionality and safety that exceed the expectations of consumers.

About Our R&D Strategy

Under "Skin Beauty INNOVATION," one of the three pillars of Shiseido's R&D strategy, we are working to accelerate research in the area of skin foundation, which aims to elucidate the association of the skin with the conditions inside the skin, such as blood vessels and lymphatic vessels, immunity, and nerves, as well as to elucidate the causes of and develop solutions for the eternal skin problems that our customers have been troubled with for many years, such as dark spots / dullness, wrinkles, facial sagging, and pores. To this end, we have advanced our analytical technologies for active ingredients on the superficial and inner layers of the skin, as well as skin measurement and evaluation methods.

- Integrated Report 2022 (Beauty Innovation)
  https://corp.shiseido.com/report/en/2022/value_creation/innovation/
- Keywords

Skin Beauty INNOVATION, analytical technology, penetration

<Reference>

Researchers' challenge

■R&D Philosophy "DYNAMIC HARMONY" approach

This research was carried out under the Inside/Outside approach of Shiseido's R&D philosophy, DYNAMIC HARMONY. The cutting-edge technology, which can capture how active ingredients penetrate or are distributed inside the skin, will lead to the development of beauty solutions that will bring about effects on the skin surface like we have never seen before.

Researcher Keishi Kihara

■We want to convey to our customers how ingredients penetrate into the skin in an easy-to-understand manner and help them feel the effects even better

The imaging technology we have developed nearly 10 years ago for visualizing the penetration of ingredients inside the skin has been utilized for many products as a tool to convey the quality of the developed products to our customers in an easy-to-understand manner. On the other hand, the resolution of the conventional technology was not high enough, and it has been our researchers' strong desire to "convey the state of ingredients penetration using a higher resolution technology and help the customers realize the high efficacy." This is what led to the results of the present study.

NanoSIMS, the analytical technology that we focused on in this study, is a cutting-edge observation method that allows for the visualization of the distribution of ingredients in an ultrafine space smaller than cells. However, it is difficult to operate, requires advanced skills, and involves pretreatment and analysis of biological samples for which a lot of know-how and experience are required. For these reasons, the technology had rarely been used in cosmetic research and development. Indeed, in the process of developing the present technology, we repeated trials and errors a number of times until satisfactory data could be obtained. Although it was not a smooth path, we persistently continued our study believing that the analysis and new product development far superior to the conventional technologies would be possible. Finally, after 3 years, we were able to evaluate penetration of active ingredients in the skin tissue and compare it between formulations.

Shiseido's R&D Philosophy "DYNAMIC HARMONY"

- Shiseido Formulates Its Unique R&D Philosophy "DYNAMIC HARMONY" (2021)
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- DYNAMIC HARMONY website:
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