

**Press Release** 

## **Research and Development**

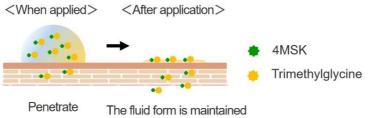
# Shiseido Develops "4MSK/Fluid Penetration Technology" Penetrating Brightening Effective Ingredient 4MSK into Skin

Shiseido has developed the "4MSK/fluid penetration technology", which enhances the penetration of the company's uniquely developed brightening effective ingredient, 4MSK (4-methoxysalicylic acid potassium salt)<sup>\*1</sup> into the skin. This innovative technology combines 4MSK, which is solid at room temperature, with other ingredients to liquefy it, allowing it to remain in a fluid form even after application on the skin (Figure 1). It has been confirmed that, with this technology, the amount of 4MSK that penetrates into the skin is increased and brightening effect enhanced. The results of this study were partly presented at the 32nd IFSCC<sup>\*2</sup> Congress in London (September 19-22, 2022). The paper<sup>\*3</sup> contributed to the IFSCC Magazine (2023) following the presentation won the Henry Maso Award for 2024, an award given to young researchers. In the future, Shiseido will apply the new penetration enhancement technology developed in this study to offer safe and secure high-performance skin care products with an excellent penetration ability.

\*1 An ingredient approved by the then Health, Labour and Welfare Ministry of Japan in 2003 as a quasi-drug effective ingredient for suppressing melanogenesis and preventing dark spots and freckles.

\*2 IFSCC: The International Federation of Societies of Cosmetic Chemists

\*3 A. Okishima, T. Okamoto et. al., IFSCC Magazine, 26 (1)71-75 (2023) IFSCC



with long-lasting penetration

Figure 1: "4MSK/fluid penetration technology" combined with trimethylglycine increases penetration of 4MSK into the skin

#### Research background

In addressing the longing for a "bright skin" among consumers, Shiseido has been developing effective brightening ingredients one after another since the 1990s, introducing numerous products formulated with these ingredients. In recent years, however, as the means to achieve bright skin diversified with the expanding cosmetic medical market, the company identified the need to strengthen technologies that enhance the penetration of brightening effective ingredients in order to develop safe and highly effective products for skin brightening.

#### Inspired by "ionic liquids"

As Shiseido engaged in tasks to accomplish its goal, the company focused on "ionic liquids" that have drawn attention in the field of chemistry in recent years. An ionic liquid is a new type of liquid composed of an ionic substance having a high melting point (temperature at which a solid melts and turns into a liquid) combined with another ionic substance also having a high melting point, that becomes liquid at temperatures lower than the melting points of the original substances (Figure 2). Shiseido envisioned that, by combining 4MSK, which is solid at room temperature, with other substances to form ionic liquids, it would be possible to maintain its liquid properties even on the skin. To this end, the company set out to search for substances that can, when combined with 4MSK, turn the ingredient into fluid form.

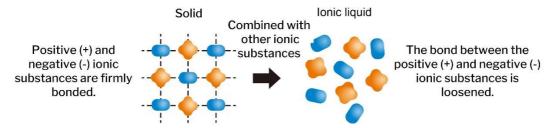


Figure 2: "Ionic liquid" that inspired this research

# "4MSK/fluid penetration technology" realized by combining 4MSK with trimethylglycine

Shiseido examined over 100 different substances and their compositions to determine the optimal combination with 4MSK. As a result, it found that 4MSK becomes liquid when combined with the moisturizing ingredient trimethylglycine at the optimum blending ratio (Figure 3). The company then confirmed that, when the two ingredients were blended into a formulation in this ratio, almost twice the amount of 4MSK penetrated the skin compared to a formulation containing 4MSK alone (Figure 4). This is considered to be the result of 4MSK in the formulation maintaining its fluid form. Shiseido named this technology that increases the penetration of 4MSK into the skin the "4MSK/fluid penetration technology."

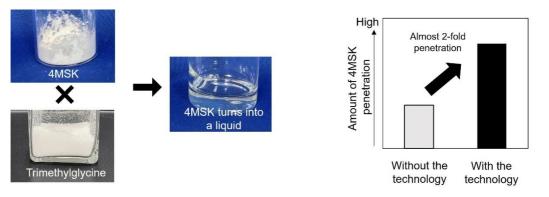


Figure 3: 4MSK becomes liquid when it is combined with trimethylglycine at the optimal blending ratio

Figure 4: "4MSK/fluid penetration technology" allows 4MSK to penetrate into the skin in high amount

## Highly effective in suppressing melanogenesis

Shiseido then examined the effect of the "4MSK/fluid penetration technology" using a three-dimensional cultured skin model. The results revealed that the technology is effective in increasing the effect of 4MSK to suppress melanogenesis (Figure 5). Moreover, with respect to the effect of 4MSK to promote exfoliation of the stratum corneum with melanin deposition, it was suggested that the use of this technology may increase this effect as well.

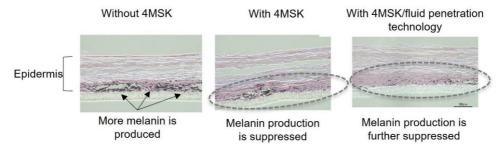
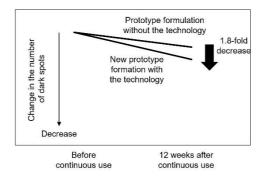


Figure 5: "4MSK/fluid penetration technology" increases the melanogenesis suppression effect

<Reference Information: Results of verification of the prototype formulation with the 4MSK/fluid penetration technology using human skin>

## Remarkable improvement on dark spots and skin brightness

The new prototype formulation with the 4MSK/fluid penetration technology decreased the number of dark spots by 1.8 fold in 12 weeks compared with the conventional prototype formulation containing 4MSK (Figure 6). The brightness of the skin also improved by 1.9 fold in 12 weeks (Figure 7).



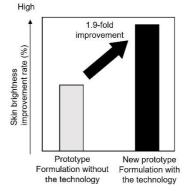


Figure 6: When the new prototype formulation with the "4MSK/fluid penetration technology" was continuously used, the rate of dark spot improvement increased

Figure 7: When the new prototype formulation with the "4MSK/fluid penetration technology" was continuously used, the rate of skin brightness improvement increased

# About Shiseido's R&D strategy:

This study was conducted under one of the three pillars of Shiseido's R&D Strategy, Skin Beauty INNOVATION, while pursuing functionality, safety, and security at a high level by fusing the life science field, which is responsible for the development of ingredients that bring high effects, and material science, which aims to increase the added values of customers such as usability and ease of use of products.

- Integrated Report 2023 (Beauty Innovation)

https://corp.shiseido.com/report/en/2023/message/cmio/ - Keywords

Skin Beauty INNOVATION, skin care, penetration

## Reference

News Release

(1) Shiseido develops a new penetration enhancing ingredient that can dramatically improve drug penetration into the skin (2022)

https://corp.shiseido.com/jp/news/detail.html?n=0000000003496 (Japanese)

#### **Researchers' Challenges**

There are some effective ingredients that cannot easily penetrate into the skin, despite having highly promising effects. To date, Shiseido has explored various approaches to improve their penetrability.

However, those approaches were not satisfactory, as there were concerns about the risk of damaging the original function of the effective ingredients, as well as the impact on the barrier function of the skin. This time, using a precise combination of our original substances, the company successfully developed an innovative technology that enables ingredients to penetrate the skin more efficiently without altering their molecular structure, while also preserving the skin's barrier function.



Anna Okishima, Ph.D., Researcher

This breakthrough is an important development that opens up new possibilities for future cosmetic development from the perspective of

combining the structural stability of effective ingredients and their penetration into the skin. Going forward, Shiseido will continue to challenge itself to developing technologies that exceeds consumer expectations by achieving both safety and efficacy.



At the award ceremony for the Henry Maso Award for 2024 (During the 34th IFSCC Congress 2024 Brazil Iguazu Falls / Researcher Okishima on the left)