

Shiseido Discovers that Magnesium Ion Promotes Hyaluronic Acid Production and Cytoprotective Effects

~Evolutionary approach to beautiful skin by focusing on minerals~

Shiseido Company, Limited (“Shiseido”) in collaboration with Professor Akira Ikari of Gifu Pharmaceutical University has discovered that magnesium ions (Mg^{2+})*¹ act on epidermal cells to promote cellular hyaluronic acid production and induce spermidine*² production, protecting the cells from oxidative damage such as UV rays (Figure 1). In our previous research, we had found that magnesium has the effect of restoring skin barrier, and in this round of research, we have clarified its moisturizing and protective effects along with their mechanisms, indicating the possibility of an unprecedented skincare solution focused on magnesium. Part of these research results were presented at the Joint Annual Meeting of the Japanese Society of Hospital Pharmacists Tokai Block and the Pharmaceutical Society of Japan Tokai Branch held on November 21, 2020 and at the Annual Meeting of the of the Japanese Biochemical Society Chubu Branch held on May 22, 2021. The results were also partly published in the December 2021 issue of the International Journal of Molecular Sciences*³.

We have conducted this research under the Inside/Outside approach of our R&D philosophy, “DYNAMIC HARMONY”. We will continue our research in a bid to provide products and services that bring out the natural beauty from both inside and outside the skin by clarifying the skincare effects of magnesium, a mineral that is abundantly present in foods and other areas in our daily lives.

*¹ A type of mineral that is abundant in the body and in foods and essential for maintaining human health. It is an auxiliary factor for more than 300 enzyme systems that control various biochemical reactions in the body (protein synthesis, muscle and nerve functions, blood sugar control, blood pressure regulation, etc.).

*² A type of compound called polyamine that is necessary in the body, involved in the growth, proliferation, and function of many cells. It is also known to have antioxidant properties.

*³ Marunaka K et al. (2021) International Journal of Molecular Sciences 23(1): 71

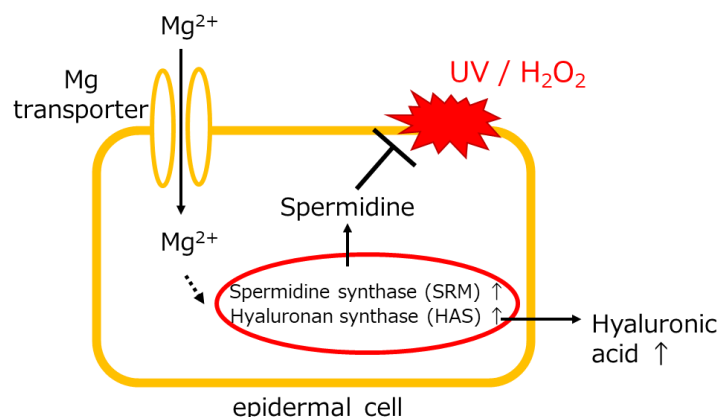


Figure 1. Magnesium ions act on epidermal cells to promote production of cellular hyaluronic acid and spermidine.

Research background

We at Shiseido have been studying the effects of minerals on the skin for more than 20 years and have already revealed that the barrier function can be restored by applying magnesium ions onto the skin. Given that magnesium transporter^{*4} has been reported to be involved in some skin diseases, we conducted research focusing on magnesium and magnesium transport via transporters in the epidermis to search for new effects of magnesium ions, which are abundant in cells.

^{*4} A magnesium transporter is present in the cell membrane and responsible for absorbing magnesium ions to the intracellular environment from the extracellular environment.

Magnesium ions promote Hyaluronic acid production

We cultured epidermal cells in a medium supplemented with magnesium chloride ($MgCl_2$) and found that the expression of hyaluronan synthase elevated and the actual production of hyaluronic acid by cells was promoted. On the other hand, when $MgCl_2$ was supplemented to the epidermal cells in which magnesium transporters were not functional, hyaluronic acid production was not promoted (Figure 2). These results suggest that hyaluronic acid production is promoted as the epidermal cells absorb magnesium ions to the intracellular environment via magnesium transporters.

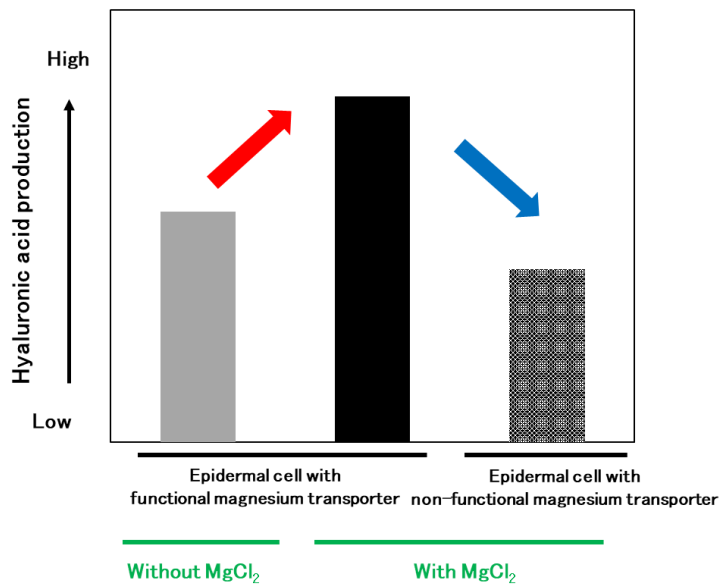


Figure 2. Supplementation of $MgCl_2$ increases cellular hyaluronic acid production.

Magnesium ions induce spermidine production and cytoprotective effects

We conducted a comprehensive search for substances that are affected by magnesium ions in epidermal cells by using microarrays^{*5}, etc., and found that the supplementation of $MgCl_2$ elevated the expression of spermidine synthase (SRM) (Figure 3). We then conducted a test in which we gave epidermal cells stimulation by UV irradiation and oxidative damage by hydrogen peroxide, and it was confirmed that in the cells cultured with $MgCl_2$, the cell viability rate after UV irradiation and hydrogen peroxide stimulation increased versus the control group without $MgCl_2$ (Figure 4). In other words, we confirmed that magnesium ions have the cytoprotective effect.

^{*5} A method for comprehensive analysis of changes in expression of various genes in a sample.

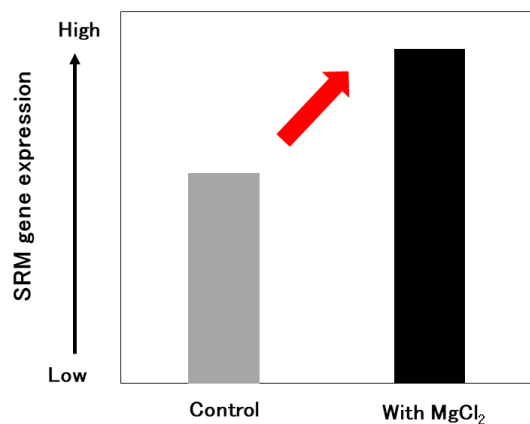


Figure 3. Spermidine synthase expression increases in the epidermal cells supplemented with MgCl₂.

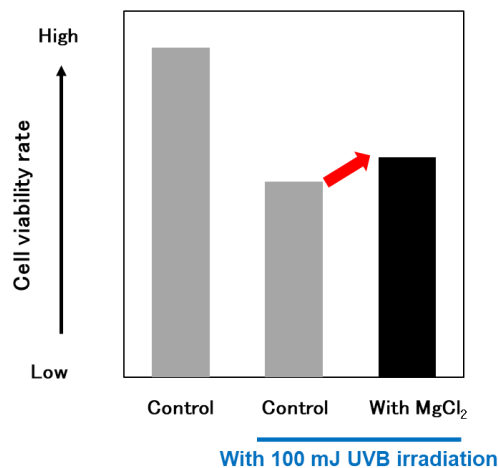


Figure 4. Cytoprotective effect against UVB damage by magnesium ions.

Future Prospects

In this study, we found that magnesium, a type of mineral, acts on epidermal cells, promoting the production of hyaluronic acid, which has the function of maintaining skin moisture and flexibility, while also inducing spermidine synthesis, a type of polyamine that is attracting attention for its antioxidant activity, and reducing damage caused by UV rays and oxidative stress. We will widely apply these results to our skincare product development. We will also continue our research on minerals, which are widely present in nature and play an important role in maintaining human health, and apply these findings to beauty innovations that help people realize healthy skin.

Shiseido's 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/>

<Reference>

Researchers' challenges

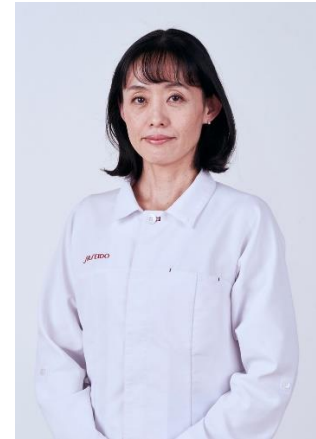
- Our pursuit for the skincare effects of minerals that are still full of mystery.

Minerals such as magnesium are indispensable components of living organisms, along with vitamins, and their various functions have already been clarified. The skincare effect of mineral-rich hot spring waters has been a well-known example. However, the mechanism by which minerals act on the skin remains largely unclear. To date, we have continued our research on minerals and skin, and have revealed that the barrier function restores by applying magnesium ions onto the skin. Since

magnesium ions are abundant in cells, we thought that magnesium ions might have other effects on the skin and conducted research focusing on magnesium, one of the most important minerals.



Researcher, Yuji Katsuta



Researcher, Makiko Goto

- Combining the expertise of professionals specialized in different human organs

Magnesium is absorbed and discharged in the small intestine and kidneys, and many researchers have studies on its mechanism. In 2018, we started joint research with Professor Ikari of Gifu Pharmaceutical University, who has extensive knowledge of magnesium functions in the kidneys and other organs, and pursued research by combining Shiseido's findings on skin cells. Cells, which are the building blocks of the body, do not necessarily work in the same way between the kidneys and the skin. Some factors work in common while others function only in a particular type of cell. In our study, we went through difficulties, failing to obtain the experimental results as we had expected that different cells might be involved, however, we found that magnesium performs different functions in different cells. It was a very interesting and important discovery.

- Realizing healthy skin with minerals

Magnesium is one of the components that are often deficient in living organisms. By taking it orally through diet as well as supplementing it onto the skin, we may achieve healthy skin. We expect that in addition to magnesium, various other minerals also function in the skin. Going forward, we want to contribute to supporting people to realize their own beauty by clarifying the effects of various minerals on the skin and leading to an optimal mineral environment.