# News Release

November 30,2023

mandom

# Mandom discovers that Potassium Alum, known to be found in hot spring water, promotes the proliferation of human epidermal keratinocytes

## —Bringing out the natural power of the skin for plump and densely firm skin—

Mandom Corporation (Head office: Osaka City, President Executive Officer: Ken Nishimura, hereinafter referred to as Mandom) conducted research at the Laboratory of Advanced Cosmetic Science of the Graduate School of Pharmaceutical Sciences in collaboration with Professor Ken Ishii of the Division of Vaccine Science of the Institute of Medical Science, the University of Tokyo (formerly the Invited Project Leader of Laboratory of Mockup Vaccine of the National Institutes of Biomedical Innovation, Health and Nutrition), with the goal of developing technology to maintain the health and beauty of skin, and it discovered that Potassium Alum, an activator of TRPM4 and known to be found in hot spring water, promotes the proliferation of human keratinocytes.

In addition, it is known that skin conditions worsen when the environmental temperature is low. It was also revealed that Potassium Alum can improve the reduced proliferation of human keratinocytes under low-temperature culture conditions.

Mandom will apply the results of this research to the development of products that maintain skin homeostasis and create healthy and beautiful skin.

The results of this research were presented at the 8th ICPAPS 2023 and the 14th Annual Conference of ISCC[*1] held in Yogyakarta, Indonesia, from November 3rd (Friday) to 5th (Sunday), 2023. We also plan to make a presentation at the 101st Annual Meeting of the Physiological Society of Japan, which will be held from March 28th (Thursday) to 30th (Saturday), 2024.

### Background of the research

Up to this point, Mandom has discovered that Potassium Alum, which is known to be found in hot spring water, activates TRPM4, which is a type of TRP channel,[*2] or sensory apparatus for the cell, present in human epidermal keratinocytes, and suppress inflammatory signals from human epidermal keratinocytes and improves skin moisture content and firmness indicators when formulated in lotions; Mandom has revealed that Potassium Alum suppresses skin inflammation and improves skin condition. However, aside from the above, effects of Potassium Alum on the

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inside of the skin remain still unknown.

Therefore, we focused on how Potassium Alum affects the firmness and plump appearance of the skin, and in this study, we confirmed the effect of Potassium Alum on human keratinocytes.

## 1.Potassium Alum promotes proliferation of human keratinocytes

Human epidermal keratinocytes form a healthy epidermis through repeated cycles of proliferation and keratinization (turnover). However, the proliferation capabilities of human epidermal keratinocytes is known to decline with age.

For this research, we investigated the effect of activating TRPM4 on the proliferation of human keratinocytes. We found that the proliferation of human keratinocytes was promoted by adding Potassium Alum, a TRPM4 activator, and BTP2, a known TRPM4 activator. In addition, this proliferation-promoting effect was inhibited by Glibenclamide (GLB), a known inhibitor of TRPM4 (Figure 1).

These facts revealed that Potassium Alum promotes the proliferation of human keratinocytes by activating TRPM4.

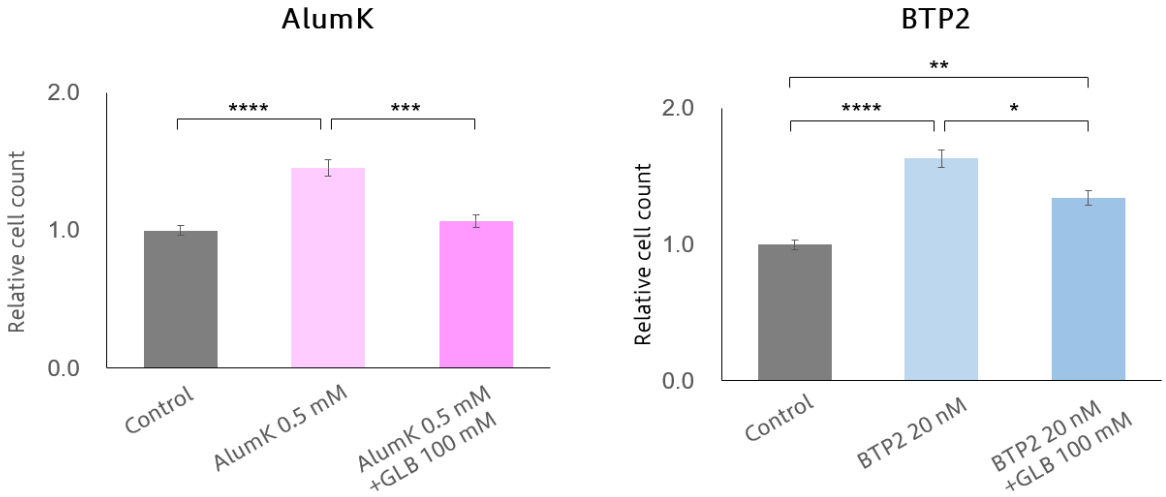


**Figure 1. Effect of TRPM4 on the proliferation of human keratinocytes**

The cell count after 48 hours of cell culture is shown. Relatively calculated with the control cell count as 1.
AlumK, BTP2: TRPM4 activators, Glibenclamide (GLB): TRPM4 inhibitor
**** p<0.0001, *** p<0.001, ** p<0.01, * p<0.05, One way ANOVA with Turkey's test

## 2. Potassium Alum improves the proliferation of human keratinocytes that is suppressed under low-temperature culture conditions

It is known that the proliferation of human epidermal keratinocytes is also affected by temperature.

When we experimented with different culture temperatures, we confirmed that the proliferation of human keratinocytes was reduced under low-temperature culture conditions (35℃) compared to normal-temperature culture conditions (37℃) (Figure 2). It was also revealed that the reduced cell proliferation under low-temperature culture conditions was improved by adding the TRPM4 activators, Potassium Alum and BTP2 (Figure 3).

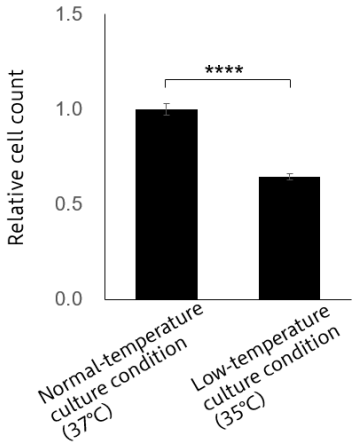


**Figure 2. Effect of temperature on the proliferation of human keratinocytes**

The cell count after 48 hours of cell culture is shown.
Relatively calculated with the cell count at 37℃ as 1.
**** p<0.0001, Student's t-test

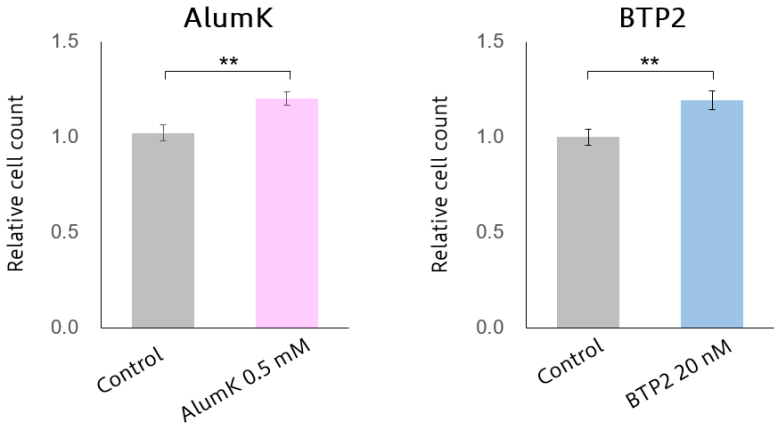


**Figure 3. Effect of TRPM4 activator on the proliferation of human keratinocytes under low-temperature culture condition (35℃)**

The cell count after 48 hours of cell culture is shown. Relatively calculated with the control cell count as 1.
Potassium Alum, BTP2: TRPM4 activator
** P<0.01, Student's t-test

The above results revealed that Potassium Alum promotes the proliferation of human keratinocytes by activating TRPM4.

At Mandom, we aim to apply the results of this research to develop products that bring out the innate power of the skin by adjusting the turnover rate of human epidermal keratinocytes and supporting the skin's ability to regenerate itself, resulting in skin that is plump and firm.

Notes and glossary

*1 The 8th ICPAPS 2023 and The 14th Annual Conference of ISCC
The 8th International Conference on Pharmacy and Advanced Pharmaceutical Sciences （ICPAPS 2023） and the 14th Annual Conference of the Indonesian Society for Cancer Chemoprevention （ISCC 2023）

*2 TRP = Transient Receptor Potential
Belongs to the cation channel family involved in various sensory reception, and is a sensor that detects chemicals, temperature, etc. and converts them into electrical signals