Mandom's discovery: Potassium alum inhibits activities of the cell sensors TRPV1 and TRPA1 and decreases pain and sensory irritation

Mandom Corporation (head office: Osaka City, President Executive Officer & Director: Motonobu Nishimura; hereinafter referred to as "Mandom") and the National Institutes of Biomedical Innovation, Health and Nutrition (Ibaraki City, Director General: Yoshihiro Yoneda; hereinafter referred to as "NIBIOHN") have been engaged in collaborative research to develop technologies to control pain and inflammation. The specific aim for Mandom has been to develop technologies to maintain health and beauty of the skin and for NIBIOHN to develop technologies for highly effective and less painful vaccines.

Mandom and the project leader of the NIBIOHN Laboratory of Mockup Vaccines, Dr. Ken Ishii (professor of the Institute of Medical Science, the University of Tokyo), discovered that potassium alum (aluminum ion) inhibits the activities of TRPV1 and TRPA1, members of the Transient Receptor Potential (TRP) channel*1 family of cell sensors. We also found that a higher concentration of potassium alum and lower pH better inhibit the TRPV1 and TRPA1 activities. We confirmed that pain and sensory irritation tend to be alleviated by inhibiting the activities of TRPV1 and TRPA1, which are known as sensors for pain and sensory irritation.

Our previous study has shown that potassium alum activates TRPM4 and thereby has an inhibitory effect on inflammatory signals produced by keratinocytes (news release of May 28, 2019).

The results of our present study were published in the Proceedings of the 97th Annual Meeting of the Physiological Society of Japan, March 17-19, 2020

This study was conducted with the cooperation of Professor Makoto Tominaga of the Exploratory Research Center on Life and Living Systems at the National Institutes of Natural Sciences, (formerly Okazaki Institute for Integrative Bioscience).

1. Potassium alum has an inhibitory effect on pain and sensory irritation

Potassium alum is known as an ingredient in hot springs and is said to have an inhibitory effect on pain and inflammation. Its mechanism, however, had been unknown. Our previous studies on TRP channels have shown that potassium alum activates TRPM4 in the skin and inhibits the immune response of keratinocytes. Thus, our present study examined the effect of potassium alum on skin sensations by investigating its effect on TRP channels expressed in sensory nerves.

2. Potassium alum inhibits the activities of TRPV1 and TRPA1, which function as pain sensors

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Mandom has previously reported on various functions of TRPV1 and TRPA1, receptors which respond to pain and irritants. Our present study found that potassium alum inhibited the activities of TRPV1 and TRPA1 among TRP channels expressed in sensory nerves. This inhibitory effect was shown to be concentration dependent (the effect increased with higher potassium alum concentrations) (Figure 1) and pH dependent (the effect increased under acidic conditions and decreased approaching and near neutral) (Figure 2). The pH dependency is thought to be due to the increased solubility of potassium alum under acidic conditions.

3. Potassium alum tends to alleviate pain and sensory irritation of the skin

Our present study was conducted on 11 Japanese male and female volunteers (5 males and 6 females) using microneedle sheets*2 (with and without potassium alum) applied around their left and right eyes for 30 minutes. The strength of the sensory irritation was evaluated from 15 to 30 minutes after sheet placement.

When the participants compared the sheets “with potassium alum” with those “without potassium alum,” 64% responded that the side “without potassium alum had a somewhat stronger irritating sensation,” 18% responded that the side “with potassium alum had a somewhat stronger irritating sensation” and 18% responded, “No difference.” (Figure 3).

These results suggested that potassium alum alleviates pain and sensory irritation by inhibiting TRPV1 and TRPA1 activities.

NIBIOHN is applying the research results to elucidate more information on the immune system of the skin and the relationship between TRP channels and inflammation and to develop technologies for highly effective and less painful vaccines. Mandom is applying the results to develop cosmetics that are comfortable to use and without sensory irritation.

***1 TRP=Transient receptor potential**

TRP channels are a family of cation channel proteins involved in various types of sensory reception and are sensors which convert sensations, such as from chemical substances and heat, into electrical signals.

Achievements of Mandom

1. Evaluation of sensory irritation using irritant receptors: novel method development in the cosmetics industry by Mandom to develop gentler skin products (October 9, 2007)
2. Mandom identifies the relationship between sensory irritation and irritant receptors in the skin-First time in the cosmetics industry (September 22, 2010)
3. Discovery of reduced hair coloring sensory irritation using carbonate ions by Mandom (December 6, 2010)
4. Role of the eucalyptus-derived ingredient eucalyptol in reducing unpleasant sensory irritation from cooling sensations (March 8, 2012)
5. Identification of a mechanism by Mandom to perceive cold temperature as cold change (October 18, 2012)
6. Discovery by Mandom of a highly effective approach to reduce the unpleasant irritation associated with cooling sensations with a natural ingredient borneol (December 16, 2013)
7. Identification by Mandom of the mechanism by which hypo-osmotic solutions such as water cause irritation in the nasal cavity and eyes (July 9, 2015)
8. Mandom identified menthol-induced analgesic mechanisms (December 10, 2015)
9. Discovery by Mandom of the effect of the low-odor ingredient “isobornyloxyethanol” to reduce sensory irritation induced by cooling ingredients (November 20, 2018)

10. Mandom and the National Institutes of Biomedical Innovation, Health and Nutrition confirmed for the first time in Japan that TRPM4, a cell sensor, controls inflammatory reactions in keratinocytes (May 28, 2019)

***2 Microneedle sheets**

They are cosmetic sheets onto which cosmetic ingredients are formed into a very fine needle-like shape and are placed on problematic areas, such as around the eyes and mouth.

【Reference materials】

Figure 1. Inhibitory effect on TRPV1 and TRPA1 activation by potassium alum concentration

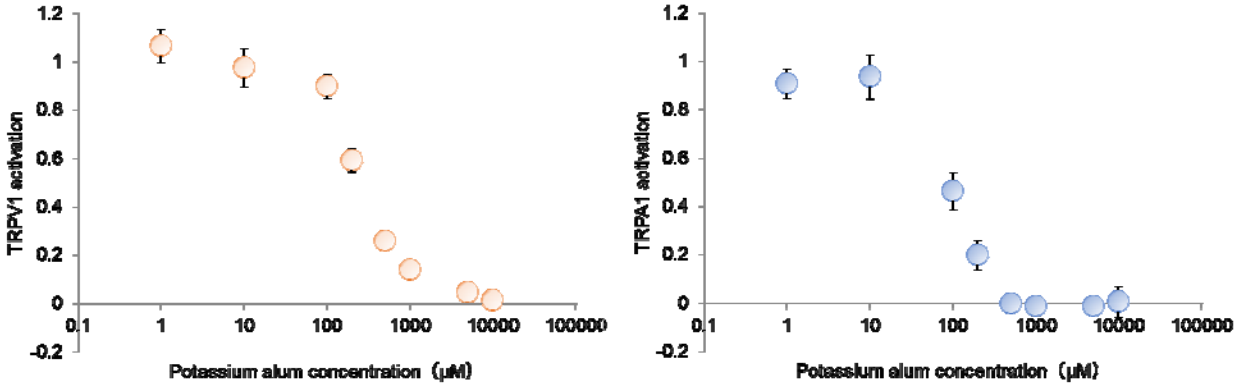

Figure 2. Inhibitory effect of potassium alum on TRPV1 and TRPA1 activities by pH

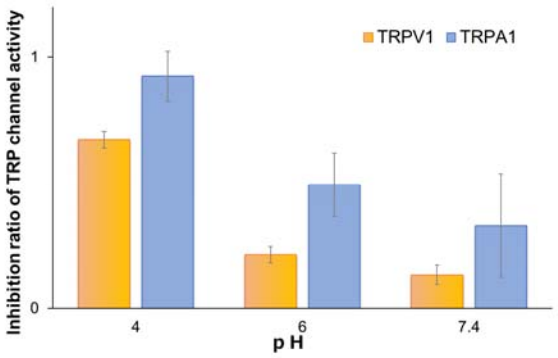

Figure 3. Evaluation of sensory irritation on the skin with and without potassium alum