

## **Evaluation of sensory irritation using irritant receptors: novel method development in the cosmetics industry by Mandom to develop gentler skin products**

- Envisioning cosmetics free of uncomfortable “tingling” and “stinging”-

The Mandom Corporation (Head Office: Osaka, President Executive Officer: Motonobu Nishimura, hereafter “Mandom”) has focused its research on establishing an “evaluation technique for elucidating pleasantness and unpleasantness” to develop “comfortable” products for customers. As part of this research, Mandom has developed an evaluation method for unpleasant “tingling” and “stinging” sensations felt on rare occasions when using cosmetics. We hope to utilize these findings at Mandom to evaluate a wide variety of products.

Furthermore, we have presented the results of this study at the “6<sup>th</sup> International Conference on Alternatives to Animal Testing (Tokyo)” held in Japan on August 25.

### **1. Background of the study**

In recent years, consumers have become increasingly conscious of safety and security, based on the fact that 60-90% of all women report having a sensitive skin. Despite recent improvements in manufacturing, and fewer cosmetics resulting in “tingling,” “stinging” or other unpleasant sensations during use, there are customers that cease using cosmetics due to sensory irritations. In addition, there are increasing number of cases where in consumers can no longer use cosmetics they have long used without problems due to sudden irritation from seasonal changes or physical conditions. Thus, sensory irritation is a major factor not only for a comfortable use of cosmetics by consumers, but also in deciding whether to use or not. However, the mechanism of sensory irritation is often not understood, and thus meaningful solutions are not proposed. Evaluation of sensory irritation has mostly involved stinging tests of human subjects. Accuracy of human-based evaluations may be improved depending on the test sites and application methods, but nevertheless, there are drawbacks, as inconsistencies are common. Also, it is difficult to increase the number of tests within a short period of time. In order to develop a technique for reducing unpleasant sensory irritations, we first require a method for precisely evaluating sensory irritation that allows for numerous tests to be conducted.

Therefore, at Mandom, we have conducted a study to develop an evaluation method for sensory irritation that does not use human skin.

\* Stinging test: a method for evaluating sensory irritation in people by applying a sample of the cosmetic to human skin.

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## 2. Perception of “pain” and “heat”

How do people sense “pain” and “heat”? People perceive noxious stimuli and temperature on the surface of the body. This information is transmitted to the brain in the form of electrical signals, and we perceive feelings of “pain” or “heat” (Fig. 1) In the superficial layer of the skin, chemical substances that cause temperature and noxious stimuli are converted to electrical signals present in the sensory nerves (Fig. 2).

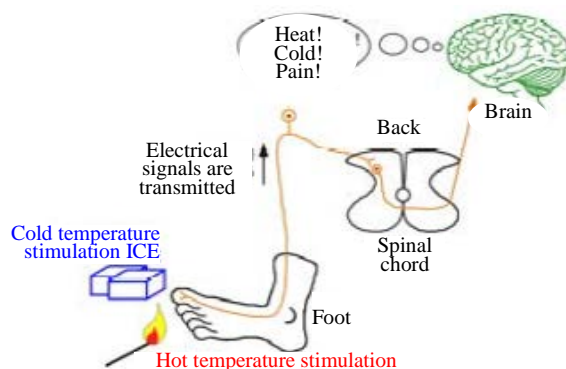


Fig. 1 Transmission of “pain” information

The mechanism by which people sense noxious stimuli and temperature was not identified several decades ago. Human irritant receptors and temperature reception are very closely related. This was discovered based on receptors that were activated by stimulation from capsaicin, the alkaloid in chili pepper. It is also activated by high temperature that causes pain. Amongst these, we have chosen to focus on a group of membrane proteins called “TRP (Transient Receptor Potential) channels,” which play a major role in the perception of noxious stimuli and temperature in humans (Fig. 3).

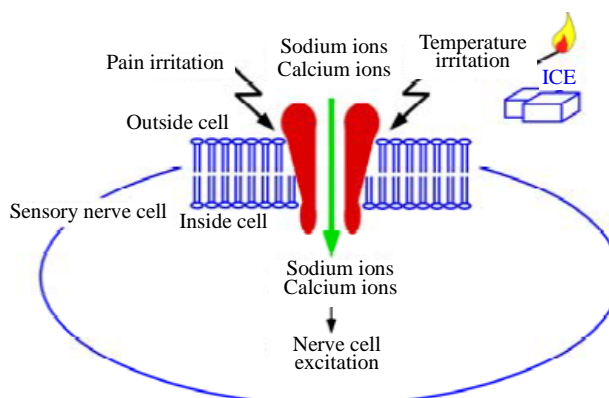


Fig. 2 Irritant receptor (receptor)

\* Noxious stimuli: A stimulation caused by irritants from outside the body.

## 3. Evaluation utilizing irritant receptors

TRP channels have recently been in the spotlight as sensory receptors in the skin and sensory nerves. TRPV1, a receptor for capsaicin (the alkaloid in chili pepper), and TRPM8, a receptor for menthol (the alkaloid in mint), are typical representatives.

In general, many of the ingredients added to cosmetics that cause sensory irritation activate the TRP channels. Examples of these include preservatives such as parabens, citric acid, lactic acid, alcohols and camphor. Based on these facts, we spent several years working on

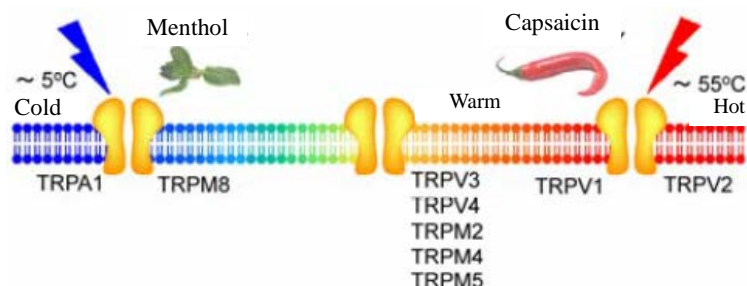


Fig. 3 Temperature and irritation-sensing TRP channels

establishing how to evaluate irritation using TRP channels. This had led to the first discovery in the cosmetics industry of a method for evaluating irritation based on these irritant receptors. This method involves transfected cultured cells to express the irritant receptors. These cells were then treated with irritants and calcium-specific fluorescent indicators were used to measure the changes in calcium concentration. By adopting the so-called “calcium imaging” technique, elevated calcium levels could be observed with high sensitivity as fluorescence intensity increased when the receptors were activated by compounds assessed for irritation. In other words, substances that cause unpleasant “tingling” and “stinging” sensations could be detected with high accuracy.

By continuing this research, we at Mandom hope to assess ingredients that may cause unpleasant “tingling” and “stinging” sensations, which are a nuisance to many women. By seeking substances that may suppress these unpleasant sensations, we hope to ensure comfortable women’s cosmetics are developed. In addition, we intend to use this technique to assess several marketable products, including hair coloring products that have slight irritation issues, and deodorants with long-lasting comfortable coolness.

We will attempt to thoroughly explore what “comfort” means to consumers, and determine how to further improve.

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