

Mandom identifies the relationship between sensory irritation and irritant receptors in the skin-First time in the cosmetics industry

-A core technique for reliable quality by Mandom-

Mandom Corporation (Head Office: Osaka, President Executive Officer: Motonobu Nishimura, hereafter "Mandom") has been developing products in pursuit of "superior feel and function" and "reliable and safe quality." In particular, in order to develop women's cosmetics, we have been attempting to develop a technique for providing customers with "reliability" and fully considering how to be gentler on the skin.

As part of this, Mandom has developed an alternative evaluation method for unpleasant "tingling" and "stinging" sensations felt on rare occasions when using cosmetics. Here, the irritant receptor TRP (Transient Receptor Potential) channels are the key to this alternative evaluation method (Fig. 5). Through joint research with Professor Makoto Tominaga of the Okazaki Institute for Integrative Biosciences, we found that these TRP channels are activated by preservatives and polyalcohols. A strong correlation exists between this activation and sensory irritation of the skin. In addition, we found that this same method can be applied to evaluate sensory irritation of products. Mandom intends to use this technique for the development of various cosmetics that may be comfortably used to an extent that was previously considered not feasible.

Furthermore, we shall present the results of this study at "The 26th Congress of the International Federation of Societies of Cosmetic Chemists (IFSCC)" held from September 20 to 23, 2010 in Argentina.

1. Background of study

(1) "Tingling" and "stinging" sensation when using cosmetics

"Tingling" and "stinging" sensation experienced when using cosmetics is referred to as "sensory irritation," and all of us have encountered such experiences. Sensory irritation and skin inflammation are likely to be regarded as similar, but there are many forms of sensory irritation with no inflammation. So, if there is sensory irritation, should one stop using cosmetics for the fear of inflammation even if there isn't any? Women in particular are experiencing an increasing number of cases in which sensory irritation is forcing them to abandon cosmetics products they had previously used with no problems. In other words, there are consumers missing out on the "health" and "beauty" benefits available from cosmetics because they are experiencing "sensory irritation."

At Mandom, we are actively conducting research to alleviate the unpleasant "sensory irritation" caused in some rare occasions by otherwise "safe" cosmetics that do not cause inflammation.

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(2) Safety and reliability

At Mandom, we categorize cosmetics quality into two: "safety" and "reliability". We define "safety" as not causing any hardship to the skin, in other words, an "essential quality", so consumers can enjoy the benefits of cosmetics without any risks.

Mandom has spent the last 80 years of its corporate history working to realize this "essential quality." Next, at Mandom, we define "reliability" as the realization of a high level of quality in products that are gentle on consumers (Fig. 1). This refers to a consumer-centric approach, and using modern techniques, such as replacing preservatives with "alkanediol" moisturizing agents, which was the outcome of many years of research, or highly accurate evaluation of sensory irritation through the pioneering use of "TRP channels" worldwide. Mandom is working to develop high quality products that prioritize "reliability" over "safety".



(3) Alternative evaluation using irritant receptors

Evaluation of sensory irritation is done by a stinging test, performed on humans. The drawbacks of human-based evaluation are that, despite the fact that accuracy may be improved through the selection of subjects, test sites and application methods, there are several inconsistencies. It is therefore, difficult to increase the number of tests within a short time. "TRP channels," are receptors of chemical irritants and temperature. Mandom has developed an alternative evaluation method for sensory irritation based on these receptors.

Mandom has spent more than five years developing this alternative evaluation method for irritation using TRP channels. We have reported that it may be possible to precisely evaluate sensory irritation via "calcium imaging" method using cultured cells that express these irritant receptors. Using this method, it is possible to detect compounds that may lead to the unpleasant "tingling" and "stinging" sensations in humans with increased sensitivity.

2. Linkage between the alternative evaluation method and sensory irritation

(1) Sensory irritation due to preservatives and polyalcohols

Mandom conducted a detailed study of the relationship between the strength of sensory irritation when cosmetics are applied to the skin and TRP channels' activation. Use of "preservatives" and moist "polyalcohol" ingredients cause irritation in rare instances. Based on the results, we discovered that the preservatives activate the wasabi receptor, TRPA1, while the polyalcohols activate the capsaicin receptors, TRPA1 and TRPV1. In addition, we found similarities to the stinging test, which is a highly accurate test to determine the level of receptor activation and sensory irritation of the skin in sensitive subjects (Fig. 2).

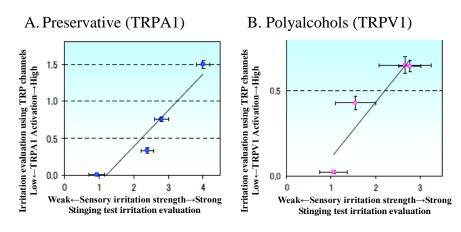
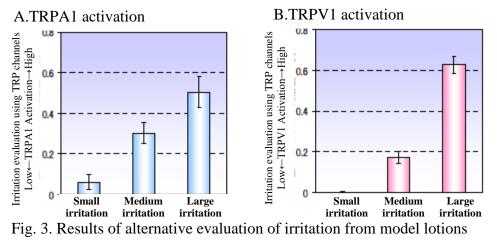


Fig. 2. Relationship between TRP channels and sensory irritation

(2) Application to cosmetics

We used the TRP channel-based evaluation method for sensory irritation to not only examine raw materials for cosmetics, but whether it is possible to evaluate the sensory irritation of cosmetics themselves. As a result of measuring the effects of three model lotions with different irritation strengths on TRPA1 and TRPV1, we observed changes in TRP channel activation depending on the strength of sensory irritation (Fig. 3). The results suggest that an evaluation using TRP channels can be adopted for cosmetics as well.



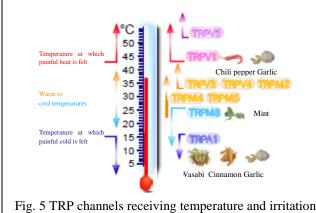
By continuing this research, Mandom hopes to assess the ingredients that cause unpleasant "tingling" and "stinging" sensations, which are inconvenient to many women. We intend to develop cosmetics for women that may truly be comfortable to use.

In addition, we are using this knowledge to develop various comfortable cosmetics that were not possible previously.

Mandom shall further explore this knowledge in order to improve the "reliable" quality from a consumer perspective.

<Sensory irritation mechanism>

Thanks to the recent progress in life sciences, we have identified the "irritation sensors" present in the neurons in the skin that sense chemical substances and temperature, convert them to electrical signals, which are key to sensory irritation (Fig. 4). "Tingling" and "stinging" sensations partly resemble temperature perception. It has been scientifically determined that we perceive irritating sensations and temperature perception via the same sensor, the "TRP channels" (Fig. 5).



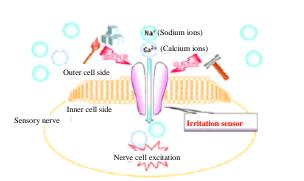


Fig. 4. Irritation sensors in sensory nerves

TRP channels have recently gained attention as receptors that act as sensors in the skin and sensory nerves. Typical examples are TRPV1, the capsaicin receptor (main ingredient in chili pepper) and TRPM8, the menthol receptor (main ingredient in mint). Many such ingredients added to cosmetics generally are thought to cause sensory irritation by activating TRP channel. Examples include citric acid, lactic acid, alcohol, and camphor.