

# Discovery by Mandom of a highly effective approach to reduce the unpleasant irritation associated with cooling sensations with a natural ingredient borneol

- Application of TRP channel research to achieve a more comfortable cooling sensation-

Mandom Corporation (Head Office: Osaka, President Executive Officer: Motonobu Nishimura, hereafter "Mandom") has been conducting studies with a focus on sensory irritation in skin, with the goal of improving the usability and function of cosmetics (quasi-drugs). Through joint research on sensory irritation with Professor Makoto Tominaga of the Okazaki Institute for Integrative Bioscience, Mandom has developed an evaluation method using TRP (Transient Receptor Potential) channels, and has applied these tests to its products (\*1).

We used TRP channels, and discovered that the natural ingredient "borneol" (\*2) is a highly effective ingredient capable of reducing the unpleasant irritation caused by freshening ingredients.

Furthermore, the results of this study were published in the Journal of Physiological Science on October 12, 2013. We also plan to present these findings at the "91<sup>st</sup> Congress of the Physiological Society of Japan" held from March 16 to 18, 2014.

## 1. Unpleasant irritation due to intense cooling sensations and the search for new ingredients to alleviate

Many freshening ingredients have been developed for use in cosmetics. Presently, *l*-menthol is one of the most commonly used, and is indispensable to achieving a strong cooling sensation. However, *l*-menthol causes a burning sensation when used in excess, and thus the unpleasant irritation. TRPA1, a receptor for the spicy ingredient in wasabi and mustard involving the TRP channels, is involved in such burning sensation, So, we at Mandom focused on TRPA1, and identified freshening ingredients that do not activate TRPA1, and hence do not cause an unpleasant irritation, or those that reduce the unpleasant irritation.

At Mandom, we previously found that the eucalyptus-derived ingredient eucalyptol is effective in inhibiting the activation of TRPA1 by  $\ell$ -menthol, and in reducing the unpleasant sensations. We searched for new ingredients that reduce unpleasant irritation effectively.

### 2. Borneol unpleasant irritation reducing effects

As a result of using TRP channels to explore new ingredients that effectively inhibit activation of TRPA1 by  $\ell$ -menthol, Mandom first discovered that borneol, a freshening ingredient activated TRPM8 (a cooling sensor), one of TRP channels, and at an intensity similar to TRPA1 inhibition by  $1/10^{\text{th}}$  concentration of eucalyptol (Fig. 1).

In addition, Mandom was able to use the neck of human subjects to test the cooling sensation and verify that borneol reduces the unpleasant irritation caused by excessive  $\ell$ -menthol. We found that this effect reduces the unpleasant irritation in a statistically significant manner (Fig. 2).

Accordingly, borneol could be an ingredient that reduces the unpleasant irritation from *l*-menthol while simultaneously providing a cooling sensation.

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In the future, we intend to pursue research on TRPA1 inhibition, and use borneol to develop new and comfortable refreshing cosmetics. Mandom is exploring this ingredient to be applied for the cooling sensations in upcoming products.

## Fig. 1. TRPA1 inhibiting effect of borneol



Fig. 2. Unpleasant irritation in the neck is reduced by borneol



## \*1 Efforts regarding TRP channels

#### <Past efforts of Mandom>

- 1. TRP channels have been identified to play major roles in the unpleasant "tingling" and "stinging" sensations felt when using cosmetics by Mandom. (released October 9, 2007)
- 2. Mandom identifies the relationship between sensory irritation and irritant receptors in the skin-First time in the cosmetics industry (released September 22, 2010)
- 3. Discovery of reduced hair coloring sensory irritation using carbonate ions by Mandom (released December 6, 2010)
- 4. Role of the eucalyptus-derived ingredient eucalyptol in reducing unpleasant sensory irritation from cooling sensations (released March 8, 2012)

#### <Sensory irritation mechanism>

Based on recent studies, "sensors" called "TRP channels" perceive chemical substances and temperature, convert them into electrical signals and are present in the nerve cells in skin. These contribute to the transmission of the sensory irritation. TRP channels have been identified to play major roles in the unpleasant "tingling" and "stinging" sensations felt when using cosmetics by Mandom. In addition, the "cooling sensation" in refreshing cosmetics is said to be attributable to the activation of TRPM8, which is a cold sensor.

#### \*2 Borneol

Borneol is a main ingredient of the Borneo camphor tree, a Dipterocarpaceae evergreen tree present on the islands of Borneo and Sumatra. It has long been used as an ingredient in perfumes, as a preservative, and in Chinese herbal medicine. It is highly volatile, and characterized by a cooling aroma that can be sensed by its smell. It has many impurities, has a low output, and yields only a small amount of product. Thus it is a scarce ingredient. It has a history of being replaced with regular camphor, which has a similar aroma.