

**Discovery by Mandom of the effect of the low-odor
ingredient “isobornyloxyethanol” to reduce sensory
irritation induced by cooling ingredients**

-Application of TRP channel research offers a comfortable cooling sensation-

Mandom Corporation (HQ: Osaka City, President Executive Officer & Director: Motonobu Nishimura, hereinafter: Mandom) has been conducting studies focused on sensory irritation of the skin, with the aim of improving both the comfort and function of cosmetics and quasi-drugs. Mandom has conducted joint research on sensory irritation with Professor Makoto Tominaga at the Exploratory Research Center on Life and Living Systems at the National Institutes of Natural Sciences, and developed an evaluation method using Transient Receptor Potential (TRP) channels, which has subsequently been applied to a number of Mandom’s products (*1). Here, we report the discovery that the low-odor ingredient “isobornyloxyethanol” effectively reduces sensory irritation induced by cooling ingredients.

Mandom is continuing to investigate the cooling technology to further develop more comfortable cosmetics.

Furthermore, we have presented these results at “The 30th Congress of the International Federation of Societies of Cosmetic Chemists (IFSCC)” held September 18 to 21, 2018. We also plan to present the results at “The 9th Federation of the Asian and Oceanian Physiological Societies Congress, in conjunction with The 96th Annual Meeting of the Physiological Society of Japan,” to be held March 28 to 31, 2019.

1. Identification of new ingredients that can reduce sensory irritation accompanied by strong cooling sensation

To mitigate the effects of summer heat, cooling cosmetics are widely used in Japan. *l*-menthol is a cooling ingredient often found in such cosmetics. However, high levels of *l*-menthol can induce a burning sensation, which can lead to unpleasant sensory irritation. This burning sensation involves activation of TRPA1, the receptor affiliated with the pungent compounds in wasabi and mustard. We therefore focused on TRPA1 in an attempt to explore inhibitors of TRPA1 activation, to reduce such sensory irritation.

We previously discovered that eucalyptol can inhibit TRPA1 activation caused by *l*-menthol, thus reducing sensory irritation. However, eucalyptol exhibits a strong odor, which often affects the fragrance of the resulting products. We sought to identify a less odorous ingredient that can also reduce sensory irritation for the development of more comfortable cooling cosmetics.

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2. Isobornyloxyethanol reduces sensory irritation

To identify less odorous TRPA1 inhibitors, we screened compounds that exhibited low volatility and had a chemical structure similar to that of eucalyptol, and evaluated the ability of the compounds to inhibit ℓ -menthol-induced TRPA1 activation. We successfully identified isobornyloxyethanol as a new TRPA1 inhibitor (Fig. 1).

Additionally, we evaluated sensory irritation on the human neck region, and confirmed that isobornyloxyethanol reduces the unpleasant irritation caused by ℓ -menthol (Fig. 2). These results suggest that isobornyloxyethanol inhibits ℓ -menthol-induced sensory irritation.

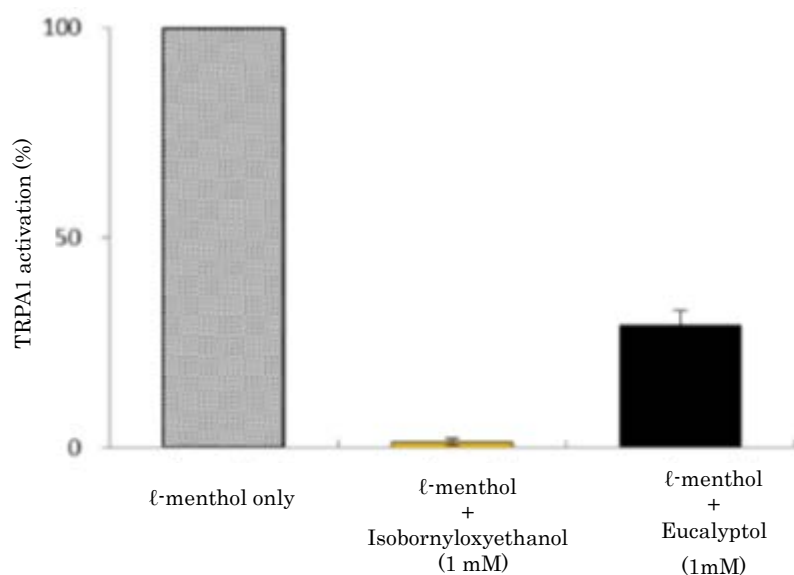
3. Isobornyloxyethanol is less odorous than eucalyptol

Results of odor intensity evaluation using an olfactory panel (*2) confirmed that the odor intensity of isobornyloxyethanol is significantly lower than that of eucalyptol (Fig. 3). Based on these results, we found that isobornyloxyethanol provides minimal impact to the overall cosmetic fragrance, and can reduce ℓ -menthol-induced sensory irritation.

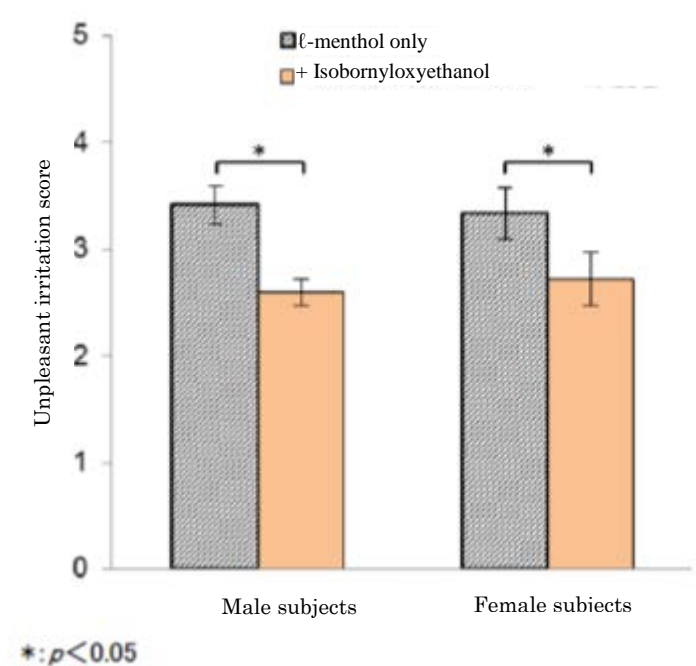
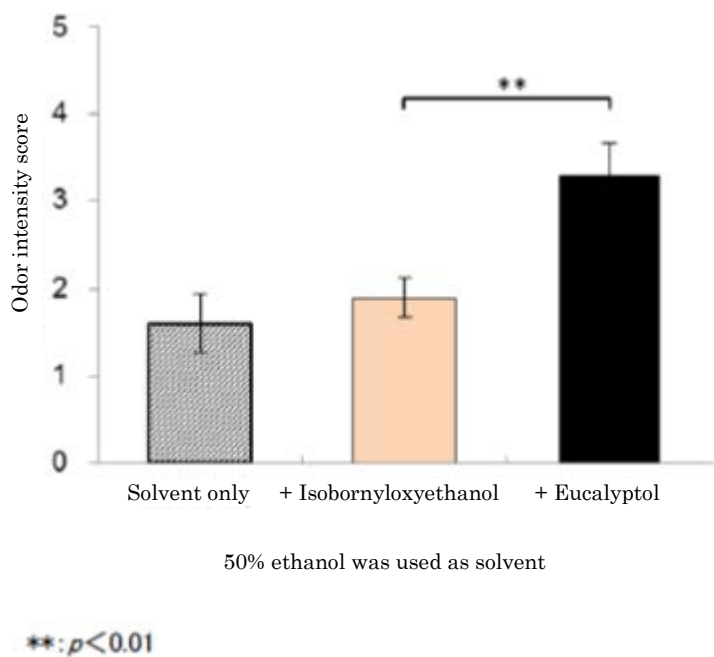
We are planning to apply the technique of reducing unpleasant irritation using isobornyloxyethanol to the development of more comfortable cooling cosmetics. In addition, we will strive to develop products that are easy to understand for consumers (e.g., by creating logos). To this end, Mandom is committed to conducting additional studies aimed at developing new cosmetic technologies.

[Reference material]

Fig. 1. Effect of isobornyloxyethanol on TRPA1 inhibition



Values are shown relative to ℓ -menthol-induced TRPA1 activation, which is taken as 100%

Fig. 2. Isobornnyloxyethanol reduced ℓ -menthol-induced sensory irritation on the neck region**Fig. 3. Odor intensity of isobornnyloxyethanol**

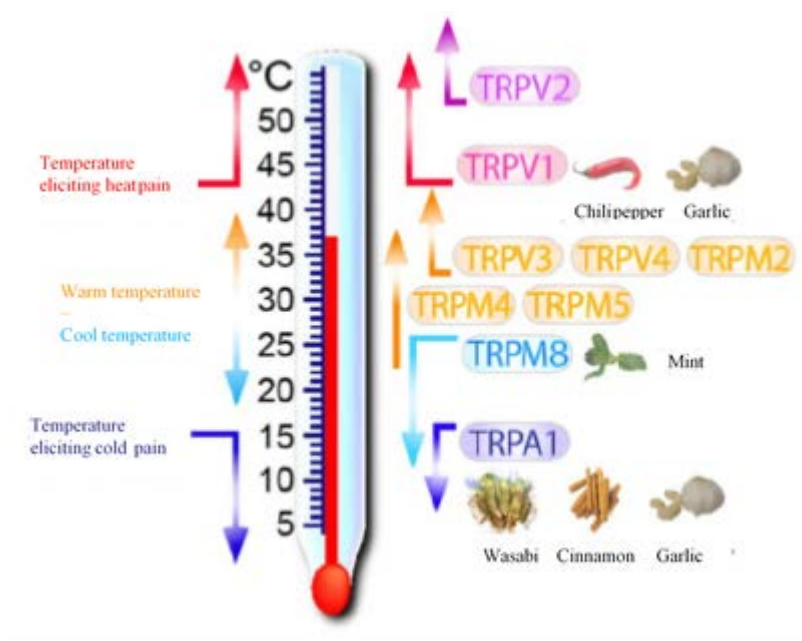
*1 Studies on TRP channels

<Previous studies at Mandom>

1. Evaluation of sensory irritation using irritant receptors: novel method development in the cosmetics industry by Mandom to develop gentler skin products (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 irritation from cooling sensations (released March 8, 2012)
5. Identification of a mechanism by Mandom to perceive cold temperature as cold change (released October 18, 2012)
6. Identification by Mandom of the mechanism by which hypo-osmotic solutions such as water cause irritation in the nasal cavity and eyes (released July 9, 2015)
7. Mandom identified menthol-induced analgesic mechanisms (released December 10, 2015).

<The mechanism of sensory irritation>

Recent studies showed that “TRP channels” (“sensors” that detect chemical substances and/or temperature and convert them into electrical signals) exist in the skin, and are involved in the perception of sensory irritation. We found that two subtypes of TRP channels, namely TRPV1 and TRPA1, play important roles in the unpleasant “tingling” and “stinging” sensations induced by cosmetic use. TRPV1 is known as the receptor for capsaicin (the main ingredient in chili pepper) and heat irritation, and TRPA1 is known as the receptor for the main ingredient in wasabi. TRPA1 plays a role in irritation induced by hair dye, preservatives and polyalcohols. On the other hand, *l*-menthol is known to activate TRPM8, the receptor for cool temperatures. Thus, the “cooling sensation” of *l*-menthol-containing cosmetics is induced by TRPM8 activation.



*2 Olfactory panel

Panel selection tests were conducted according to the “olfactory measurement method” under the supervision of odor judgment technicians. We selected panel volunteers that had high sensitivity to five types of standard odors.

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