

Mandom identified menthol-induced analgesic mechanisms.

- The useful method for evaluating sensory irritation using TRP channels -

Mandom Corporation (Head Office: Osaka, President Executive Officer: Motonobu Nishimura, hereafter “Mandom”) has been conducting studies focused on sensory irritation in the skin, aiming to make consumers feeling better as well as improving function of cosmetics and quasi-drugs when they use our products. We have been focused on the TRP (Transient Receptor Potential) channels as a one of skin sensations (Reference material * ①) collaborating with Professor Makoto Tominaga at Okazaki Institute for Integrative Bioscience. We have been developing methods to evaluate the channels’ activity, and furthermore applying our findings to our products predict unpleasant sensory irritation in the skin.

Here, we have discovered that menthol, the typical freshening ingredient, inhibits the activation of irritation sensors (TRPV1) in the dose-dependent manner. Moreover, menthol reduced the sensory irritation induced by TRPV1 activation under the sensory irritation evaluation test with human neck. Thus, we have identified a part of menthol-analgesic-mechanism, and showed that evaluating TRP channels’ activity is useful for predicating sensory irritation in skin.

We will continue to work developing safer and more secure products by applying sensory irritation evaluation methods using TRP channel.

Furthermore, the results of this study was published to the Journal of Physiological Sciences and accepted on September 16, 2015. In addition, we plan to release these findings at “The 28th Congress of the Japanese Society for Alternatives to Animal Experiments” held from December 10 to 12, 2015, and “The 93rd Congress of the Physiological Society of Japan” held March 22 to 24, 2016.

1. Analgesic effects of menthol and peppermint

Peppermint has been traditionally used in Europe and India as an herbal medicine and/or an analgesic. Menthol, the main ingredient in peppermint, is used not only a freshening ingredient in many current preparations but also as an analgesic. However, the analgesic mechanisms are still unknown.

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2. Identifying the analgesic mechanism of menthol

We have been conducted various studies on sensory irritation using TRP channels. Through the many evaluations, we focused on TRPV1 and TRPA1 as pain sensor. We previously reported that TRP channels serve as sensory irritation on skin when using cosmetics ingredients. Moreover, hypotonic condition induced sensory irritation through TRPA1 activation (Reference material*②)from the our findings. In this study, we discovered that menthol inhibits TRPV1 activation caused by capsaicin and heat stimulation (Fig. 1). Furthermore menthol inhibit TRPV1 activation in the dose-dependent manner (Fig. 2). As a result of sensory irritation tests using human neck, we discovered that menthol significantly inhibits sensory irritation caused by Vanillyl Buthyl Ether (VBE) which is one of component known as TRPV1 activator as well as capsaicin (Fig. 3).

3. Establishing a sensory irritation evaluation method

We have been focusing on TRP channels to develop safe and Credible products for consumers. We have reported that TRP channels are related to sensory irritation of the skin and eyes. Besides our findings that TRPV1 serve as analgesic mechanism induced by menthol which have been known as one of analgesic agent. We suggest that TRP channels are useful in developing methods for evaluating sensory irritation.

Fig. 1. Inhibition of TRPV1 activation by menthol

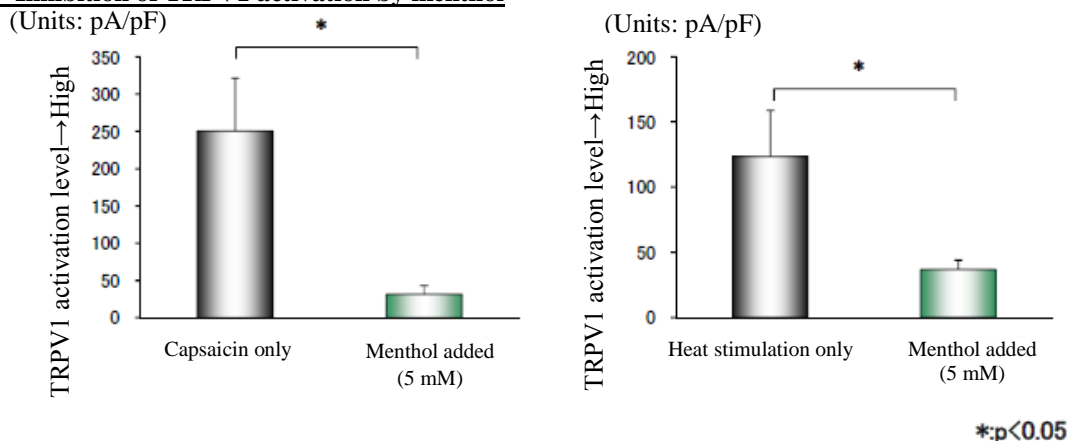


Fig. 2. Concentration-dependent inhibition of TRPV1 activation by menthol

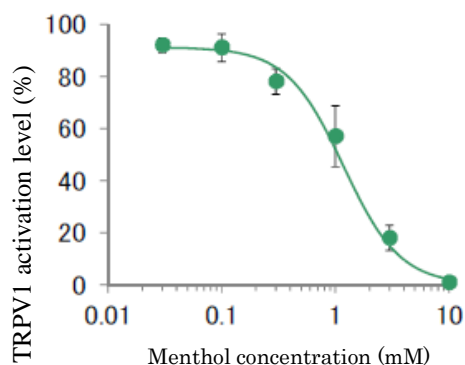
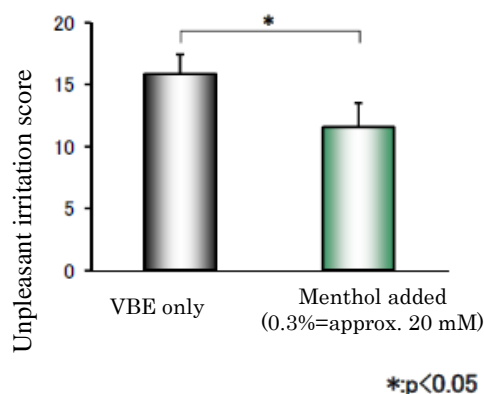


Fig. 3. Inhibition of sensory irritation by menthol

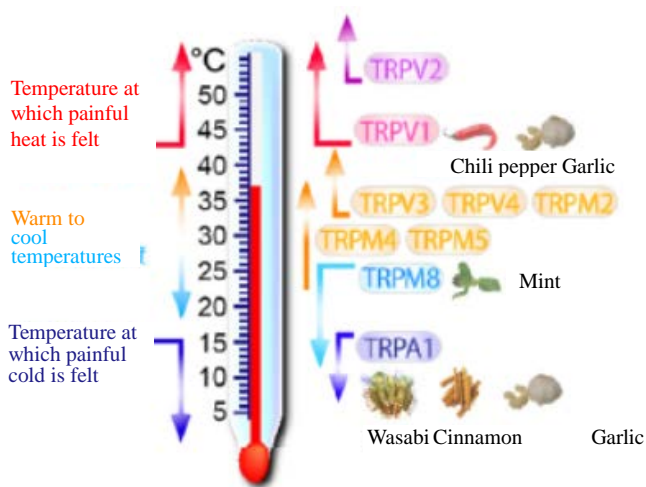


Reference material

<Studies on TRP channels>

*①<Sensory irritation mechanism>

According to recent studies, “TRP channels” (“sensors” that perceive chemical substances and/or temperature, and convert them to electrical signals) existed in the skin, and involved in the perception of sensory irritation. We found that two subtypes of TRP channels, TRPV1 and TRPA1, have important roles for feeling unpleasant “tingling” and “stinging” sensations induced by using cosmetics. TRPV1 is known as the receptor for capsaicin (main ingredient in chili pepper) and heat irritation. Furthermore, TRPA1 is known to be activated by wasabi’s main ingredient. In addition, TRPA1 also plays a role in irritation induced by hair dye, preservatives and polyalcohols. On the other hand, TRPM8 which is one of the receptor for cool temperature is known to be activated by *l*-menthol. “Cooling sensation” given by cosmetics containing *l*-menthol is induced through TRPM8 activation.



*②<Past Mandom releases regarding TRP channels>

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. Discovery by Mandom of a highly effective approach to reduce the unpleasant irritation associated with cooling sensations with a natural ingredient borneol (released 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 (released July 9, 2015)