News Release



mandom corp.

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Mandom Discovers that the Refreshing Ingredient "L-Menthyl Glyceryl Ether" has the Effect of Suppressing TRPV1 Activity

- Reducing the stress of wearing masks in everyday life during the coronavirus pandemic & realizing a refreshing feeling that lasts with little discomfort -

Mandom Corporation (Head Office: Osaka City; President Executive Officer & Director: Ken Nishimura; hereinafter referred to as "Mandom") is conducting research that focuses on sensory stimulation in the skin in an aim to improve the function and usability of cosmetics (including quasi-drugs).

Due to high external temperatures and the effects of ingredients contained in cosmetics, there are cases when unpleasant irritations such as pain and burning sensations occur on the skin. On this occasion, <u>Mandom confirmed that I-menthyl glyceryl ether (cosmetic ingredient label name:</u> <u>Menthoxypropanediol) has the effect of suppressing unpleasant irritation and is capable of maintaining a refreshing sensation</u>. In the current situation of the coronavirus pandemic, Mandom believes that this result will help the company provide consumers with a comfortable refreshing feeling that can help relieve the frustration they feel from wearing a mask during daily activities.

These findings are scheduled to be presented at the 86th SCCJ Research Symposium (online) to be held on July 15, 2021.

Background Information on this Research

Items that can achieve a refreshing sensation are being used in a wider range of scenarios that include not only hot summers when words like "intense heat" and "extreme heat" are exchanged and broadcasted every year, but also when consumers want to feel refreshed. Therefore, the things required of the term "refreshing sensation" differs depending on the item and usage scenario, such as strength and duration. At Mandom, we strive to conduct research to provide a comfortable and refreshing sensation in various situations.

L-menthol, a commonly used refreshing ingredient, has several advantages such as providing a strong refreshing feeling and has the effect of suppressing unpleasant stimuli caused by high external temperatures. On the other hand, it also has several disadvantages such as having difficulty sustaining that refreshing feeling since it is an ingredient that easily volatilizes.

This research aimed to realize a sustainable refreshing sensation with little unpleasant irritation as one of the pleasant refreshing sensations that Mandom provides.

1. Mandom discovers that I-menthyl glyceryl ether suppresses TRP (trip) V1 activity

It is known that high temperatures and some ingredients used in cosmetics cause unpleasant stimuli such as pain and burning sensations. These unpleasant stimuli involve TRPV1 (a receptor of capsicum ingredients), which is a type of TRP (trip) channel*1 that is a sensory sensor of cells.

Suppressing TRPV1 activity is effective at reducing these unpleasant stimuli. Until now, Mandom's research has shown*2 that the refreshing ingredient I-menthol has the effect of suppressing TRPV1 activity. L-menthyl glyceryl ether, whose structure is similar to that of I-menthol (see Figure 1), was discovered to have an even greater effect of suppressing TRPV1 (see Figure 2).

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2. Permeability & residualness of I-menthyl glyceryl ether to the skin

Since general-purpose I-menthol is highly volatile, the challenge lies in the low sustainability of its refreshing sensation. L-menthyl glyceryl ether, on the other hand, is considered to remain in and on the skin for a long time due to its low volatility.

When this was verified through permeability tests using skin models, it was newly confirmed that Imenthyl glyceryl ether penetrates the skin more than I-menthol and stays there longer (see Figure 3). This suggests that I-menthyl glyceryl ether can feel more refreshing for longer than I-menthol.

3. L-menthyl glyceryl ether might be able to achieve a sustained refreshing sensation & less unpleasant

irritation even when wearing a mask

Many consumers are unsatisfied*3 with the heat, stuffiness, etc., that comes with the new normal of wearing a mask throughout their daily routines due to the coronavirus pandemic. In response to this, Mandom thought that the technology it discovered during this research can be utilized to address this issue, and so the company has conducted a verification.

[Details Regarding Verification]

A comparative verification was conducted on the refreshing sensation and irritating sensation of Imenthyl glyceryl ether and I-menthol by carrying out a test that involved wearing masks that had been sprayed with a mist containing a 2.5% formulation of each ingredient (I-menthyl glyceryl ether and I-menthol). This mist was specially designed for these model masks.

[Evaluation Method]

Subjects wore non-woven masks that had dried after being sprayed on the inside with two pushes (approximately 0.2 mL) of the specially designed mist for the model masks. After 60 minutes had passed, an evaluation was conducted on the refreshing sensation and irritating sensation subjects felt as they wore the masks.

[Evaluation Results]

 Refreshing Sensation: The decrease in the score for refreshing sensation over time for I-menthyl glyceryl ether was more gradual and sustained compared to I-menthol (see Figure 4).

 Irritating Sensation: When it comes to eye irritation and skin irritation, I-menthyl glyceryl ether had a lower irritating sensation than I-menthol (see Figure 5). According to the above results, it can be said that I-menthyl glyceryl ether is an ingredient that has a less unpleasant irritating sensation and longer-lasting refreshing sensation than I-menthol.

[Considerations]

It has been found that the activation temperature threshold for TRP channels, such as TRPV1, varies according to pH. The weak acidity of the skin lowers the temperature threshold of TRP, and TRPV1 may be activated by external temperatures in the summer and temperatures within the mask, which may cause unpleasant stimuli such as burning sensations. However, it is thought that a comfortable refreshing sensation was achieved by suppressing TRPV1 activity and reducing unpleasant stimuli, such as burning sensations, thanks to blending in the refreshing ingredient I-menthyl glyceryl ether. Since consumers wear masks for long periods of time on a daily basis, and since the face is a part of the body where the skin is thin and particularly feels irritation more easily, I-menthyl glyceryl ether (which provides a lasting refreshing sensation with little unpleasant stimuli) can be said to be a suitable refreshing ingredient.

In addition, I-menthyl glyceryl ether has the characteristic feature of providing a refreshing sensation that increases when perspiring*4, and together with the aforementioned results, it can be expected to help reduce the stress consumers feel, such as the heat within their masks from having to wear their masks during daily activities in the summer time.

From these results, Mandom believes that using I-menthyl glyceryl ether with highly effective TRPV1 suppressing capabilities as a key ingredient for achieving a refreshing sensation will allow the company to provide consumers with a lasting refreshing sensation with little unpleasant stimuli.

Mandom will continue to conduct research on refreshing sensations and release products that can offer a more comfortable refreshing feeling that is more suited to consumers' usage scenarios.

*1 TRP = Transient Receptor Potential. A sensor, which belongs to a family of cation channels involved in various sensory receptor functions, that senses chemical substances, temperatures, etc., and converts them into electrical signals.

*2"Mandom identified menthol-induced analgesic mechanisms."(December 10, 2015 news release)

https://www.mandom.co.jp/en/release/pdf/2015121001_en.pdf

*3 June 2020 online survey/Mandom study on males aged 16-24/n=204

*4"Research by Mandom and application of "comfortable coolness": Effect of perspiration on cooling sensation"(April 10, 2009 news release)

https://www.mandom.co.jp/en/release/pdf/2009041001_en.pdf

[Reference Material]

Figure 1 Structures of I-menthyl glyceryl ether & I-menthol Figure 2 TRPV1 suppression effect



Figure 3 Results of skin permeability test

Amount of each compound in skin





Figure 4 Results of mask wearing test (refreshing sensation)



Figure 5 Results of mask wearing test (irritating sensation)



Unpleasantness of irritating sensation on skin