

## Mandom discovers TRPV1 inhibitory effect in specific chamomile extract

—New possibilities for reducing unpleasant irritation on sensitive skin—

Mandom Corporation (Head office: Osaka, President Executive Officer & Director: Ken Nishimura, hereinafter “Mandom”) has been conducting research in collaboration with Specially Appointed Professor Makoto Tominaga of the Nagoya Advanced Research and Development Center of Nagoya City University, focusing on cutaneous TRP (Transient Receptor Potential) channels, particularly TRPV1. TRPV1 responds to stimuli such as heat and acid and is known to be involved in the generation of unpleasant sensations such as tingling and burning.

This research revealed that environmental stressors such as atmospheric particulate matter (PM2.5) and ultraviolet rays disrupt the expression balance of factors that promote neurite outgrowth, causing excessive activation of TRPV1. This suggests that environmental stress can cause skin to become hyper-reactive and increase unpleasant irritation.

Furthermore, after looking into approximately 2,700 compounds to search for substances that inhibit TRPV1, we found that chamomile extract containing specific components is effective. In a continuous use test of a model lotion containing the extract, it was confirmed that irritation was reduced. This result will lead to the proposal of a new sensitive skin care method that stabilizes skin that has become hypersensitive due to environmental stress and provides a pleasant sensation when used. We presented the results at the 35th Congress of the International Federation of Societies of Cosmetic Chemists (IFSCC Congress), held in Cannes, France, from Monday, September 15 to Thursday, September 18, 2025.

### ■ The relationship between environmental stress and sensitive skin

Our skin is exposed to various environmental stressors on a daily basis, such as ultraviolet rays, atmospheric particulate matter (PM2.5), and dryness. It has become clear that these factors not only reduce the barrier function and trigger inflammatory reactions but also contribute to the occurrence of an “irritating sensation” such as tingling and burning.

To understand the mechanism behind this “irritating sensation,” Mandom is focusing on the sensory receptor TRPV1 present in peripheral nerves. TRPV1 is activated by stimuli such as heat and acid and plays a role in transmitting pain and discomfort.

In this study, we first confirmed the response of TRPV1 to environmental stress. First, we used PM2.5 and UVB as environmental stressors and exposed excised human skin to them. We then applied the conditioned culture medium to TRPV1-expressing cells and found that TRPV1 became more easily activated (Figure 1). Next, when keratinocytes were exposed to PM2.5 and UVB, changes in factors leading to neurite outgrowth were confirmed (Figure 2).

These results suggest that environmental stress may cause the production of substances in the skin that activate TRPV1, which in turn leads to the outgrowth of TRP channel-expressing neurons, resulting in the skin becoming hyper-reactive.



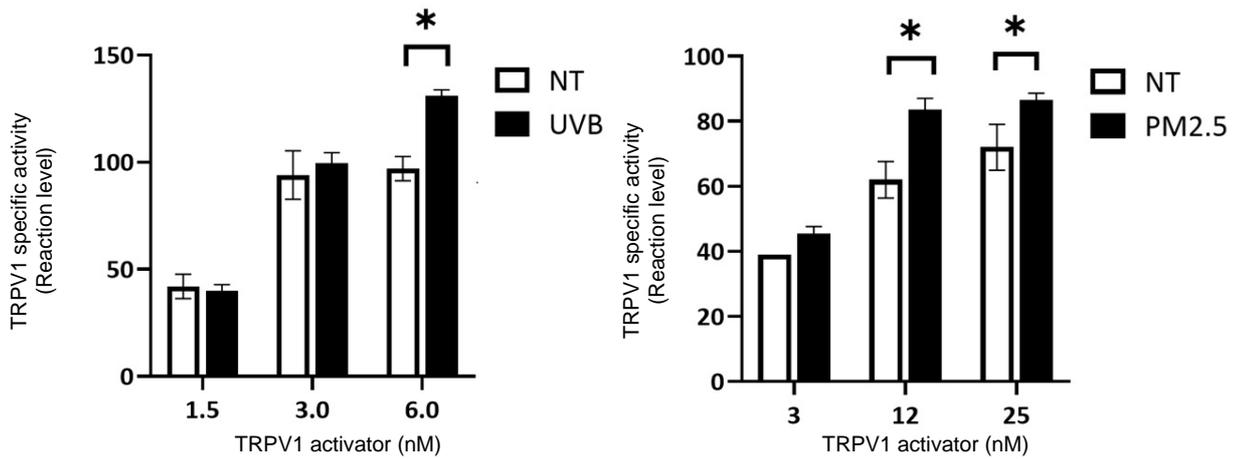


Figure 1. Changes in TRPV1 activity in culture medium after UVB irradiation and PM2.5 exposure

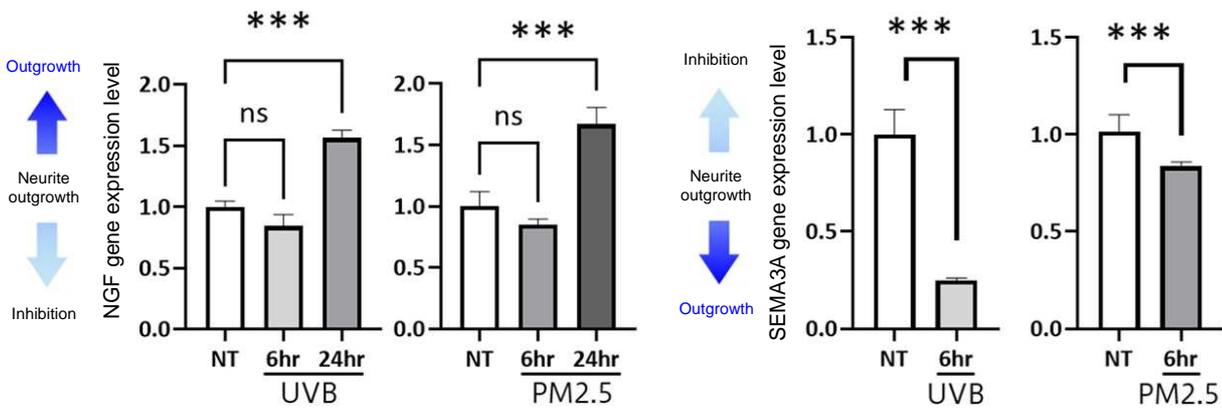


Figure 2. Changes in neurite outgrowth promoter NGF and nerve inhibitor SEMA3A in keratinocytes after UVB irradiation and PM2.5 exposure

■ **High-throughput screening to identify substances with TRPV1 activity inhibitory effects**

Aiming to develop skin care products that can be used even on hyper-reactive skin, we searched for substances that inhibit TRPV1 activity.

We established a cell line that stably expresses TRPV1 and constructed an evaluation system (high-throughput screening) that can simultaneously measure approximately 100 types of samples with high sensitivity and speed. Approximately 2,700 naturally occurring compounds were screened using this evaluation system, and it was found that chamomile (*Chamomilla recutita*) extract containing a specific substance may have the effect of inhibiting TRPV1 activity. Furthermore, analysis using calcium imaging<sup>\*1</sup> and patch-clamp<sup>\*2</sup> techniques confirmed at the cellular level that TRPV1 activity was stably inhibited (Figure 3).

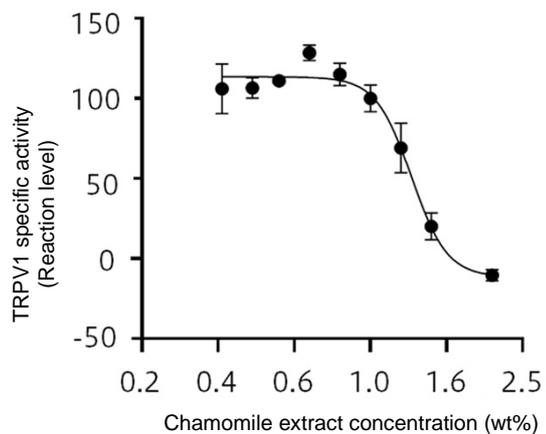


Figure 3. TRPV1 activity inhibition effect of chamomile extract

■ **Demonstrating the potential of chamomile extract containing the specific substance**

Subjects who were highly sensitive to the unpleasant stimuli caused by TRPV1 activators were selected, and a model lotion containing a TRPV1 activator and chamomile extract containing the specific substance was applied. Compared to the lotion containing no chamomile extract, the unpleasant stimuli caused by the TRPV1 activator were significantly reduced (Figure 4). This confirmed that the substance also acts as a TRPV1 antagonist\*<sup>3</sup> in humans.

Furthermore, the effectiveness of chamomile extract containing the specific substance when used continuously on sensitive skin was confirmed. First, subjects with sensitive skin were selected using a lactic acid irritation test, a widely used method for evaluating sensitivity to cosmetic irritation. They were then asked to use a lotion containing chamomile extract, which contained the specific substance, for eight weeks. This confirmed a decrease in sensitivity to irritation (Figure 5).

These results indicate that chamomile extract containing the specific substance is effective in reducing irritation in sensitive skin.

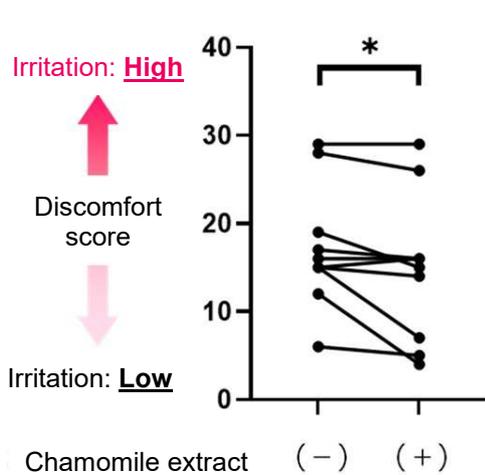


Figure 4. Changes in irritation caused by TRPV1 due to chamomile extract

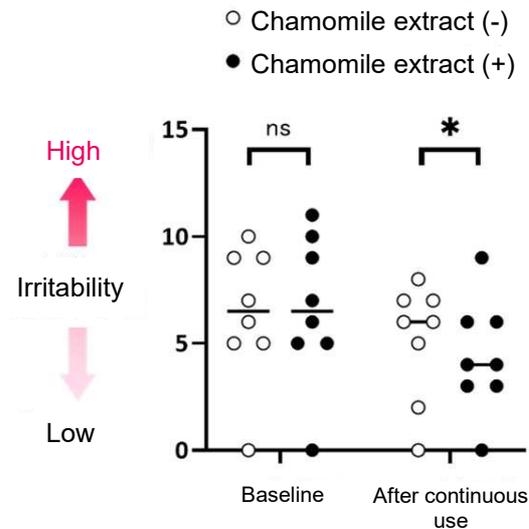


Figure 5. Changes in irritation due to continuous use of a lotion containing chamomile extract

■ **Future developments**

This study clarified the mechanism by which environmental stress worsens hyper-reactivity in sensitive skin via TRPV1 and demonstrated that chamomile extract containing a specific substance is effective in improving sensitive skin. This will enable the development of new skin care products that feel pleasant when used. Mandom will continue to promote research into skin care technologies that are in tune with the skin's senses and realize both comfort and functionality.

Remarks

- \*1 Calcium imaging: A technique to indirectly measure TRP channel activity by making calcium, which enters cells when TRP channels open, emit fluorescence, and then recording the intensity of the fluorescence in the cells as an image.
- \*2 Patch-clamp: A technique to directly measure TRP channel activity by placing a fine electrode on the cell membrane and measuring the current caused by the flow of ions through the channel.
- \*3 Antagonist: A substance that blocks the function of a receptor. Here, it refers to a substance that inhibits excessive TRPV1 responses.