

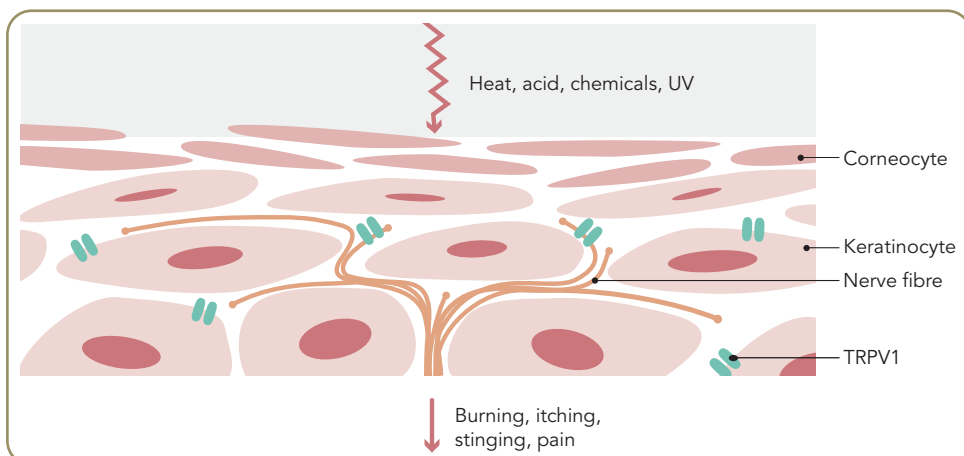
Calm skin with SensAmone P5

A novel active ingredient inspired by nature from under the sea

In the never ending search for interesting new sources for active ingredients, much of the attention these days has shifted towards ingredients of marine origin. A large number of marine species have not yet been extensively studied. This makes new findings that propose beneficial effects for us highly interesting for the cosmetics industry. One of the fascinating inhabitants of the sea is the sea anemone, known to many as the shelter for clown fish. A lesser known fact is, as the sea anemone is soft and vulnerable, it produces a venom to protect itself from predators and also to immobilise prey. Recently, scientists have found that a protein component of the *Heteractis crista* sea anemone venom is a potent inhibitor of the pain receptor TRPV1, which offers an interesting approach for sensitive skin.

The TRPV1 pain receptor is overactive in sensitive skin

The TRPV1 receptor is responsible for transmitting the sensation of pain upon contact with heat, chemicals, and acids. It is present in our skin as this is the first barrier that encounters environmental stresses. While the activity of the receptor is important to protect us from harm such as reacting with pain and withdrawing the hand when touching a hot surface, an overactivity can be harmful as well. Sensitive skin is especially characterised by a hyperreactive pain receptor which manifests itself as skin that feels too tight, itching and even burning – even though there are no harmful influences on the skin. In addition to being responsible for skin discomfort, TRPV1 is also involved in skin ageing. In photoaged human skin, TRPV1 is often overexpressed. Furthermore, constant activation of TRPV1, for example by heat and infrared radiation, leads to the upregulation of enzymes that destroy collagen in the skin, which could lead to premature skin ageing.



Therefore, the solution is to reduce TRPV1 activation in sensitive skin to normal levels to strengthen the tolerance level and to reduce the uncomfortable feeling of the skin.

SensAmone P5 - a solution for sensitive skin derived from sea anemone venom

The aforementioned sea anemone protein is a perfect candidate to help reduce skin sensitivity by inhibiting an overreaction of the TRPV1 pain receptor. However, the full-length protein is unstable and too big to penetrate into the skin and harvesting it from sea anemone venom is not feasible for cosmetic applications. Therefore, a five amino acid peptide was designed by Mibelle Biochemistry in collaboration with Venomtech, who are experts in venom-based drug discovery. This pentapeptide contains the active TRPV1 receptor binding site of the sea anemone protein. Another advantage is the sustainability through the synthetic production of the peptide which does not require sea anemones. To further ensure stability and bioavailability, the pentapeptide was incorporated into a soft sphere carrier system based on shea butter. The resulting novel cosmetic active SensAmone P5 (INCI: Pentapeptide-59 (and) Hydrogenated Lecithin (and) Butyrospermum Parkii (Shea) Butter (and) Phenethyl Alcohol (and) Ethylhexylglycerin (and) Maltodextrin (and) Aqua/Water) is a solution to relieve sensitive and irritated skin.

Efficient inhibition of the TRPV1 receptor

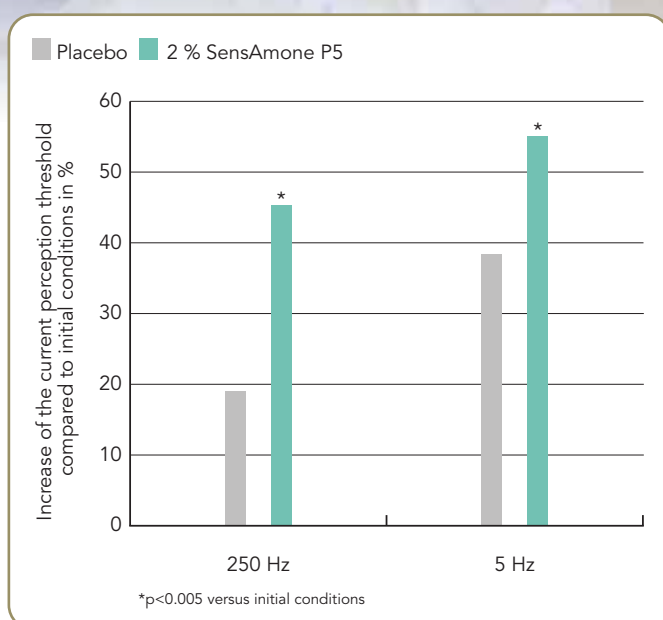
The ability of the pentapeptide to inhibit TRPV1 activation was tested *in vitro* in a whole-cell patch clamp assay. For this, a pipette containing an electrode clamps onto a cell that contains TRPV1 receptors in the cell membrane. The electrode can detect activation of the TRPV1 receptors by measuring the electrical current generated by opening of these receptors which leads to an influx of ions into the cell. When the cells were irritated by the addition of capsaicin, a potent activator of TRPV1 receptors, the activation could be measured by the increased electrical current. When the cells were treated with the pentapeptide, an 80% reduction of TRPV1 receptor activation after capsaicin treatment was observed. The inhibition of TRPV1 was even stronger than for the full-length sea anemone protein, which verifies the potency of this designed peptide. This means that the peptide is able to efficiently inhibit pain receptor activation and consequently reduce irritation reactions.

SensAmone P5 instantly reduces skin reactivity after a single application

In a double blind placebo-controlled clinical study, 31 volunteers (female, average age 47 years) with sensitive skin



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applied cream with 2% SensAmone P5 or the corresponding placebo on each side of their face. The current perception threshold (CPT) was measured using a Neurometer two hours following a single application and compared to the initial CPT before application. The Neurometer applies an electrical stimulus to the skin at different frequencies (250Hz and 5Hz) in order to target different sensory nerve cells. The CPT is then determined as the amount of electrical stimulus needed for it to be felt by the volunteer. As a result, the higher the CPT value, meaning the more electrical stimulus is needed in order

to be felt by the volunteer, the less reactive is the skin. A single application of 2% SensAmone P5 significantly increased the CPT of the skin and so reduced skin reactivity.

Long-term reduction of skin sensitivity with SensAmone P5

In addition to the short term skin soothing effect of SensAmone P5, a long term effect on the reduction of skin sensitivity was also investigated. For this, a double blind placebo-controlled clinical study was carried out in which 31 volunteers (female, average age 47 years) with sensitive skin applied a cream with 2% SensAmone P5 or the corresponding placebo on each side of their face, twice daily for a period of 28 days. To measure skin sensitivity, a lactic acid stinging test was performed by applying an aqueous 5% lactic acid solution on the nasolabial fold and assessing the stinging, burning and itching sensations on a four point scale at one minute intervals for a total period of nine minutes. Treatment with SensAmone P5 significantly reduced skin sensitivity by more than 26%. Therefore, SensAmone P5 can help to protect sensitive skin from overreacting to environmental stimuli.

SensAmone P5 is a novel cosmetic ingredient inspired by the venom of sea anemone and realised by science through the design of a pentapeptide in a shea butter based delivery system. SensAmone P5 reduces skin sensitivity and reactivity by inhibiting the activation of the TRPV1 pain receptor present in the skin. The result is a soothed and calm skin that is more resistant to environmental stresses.

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