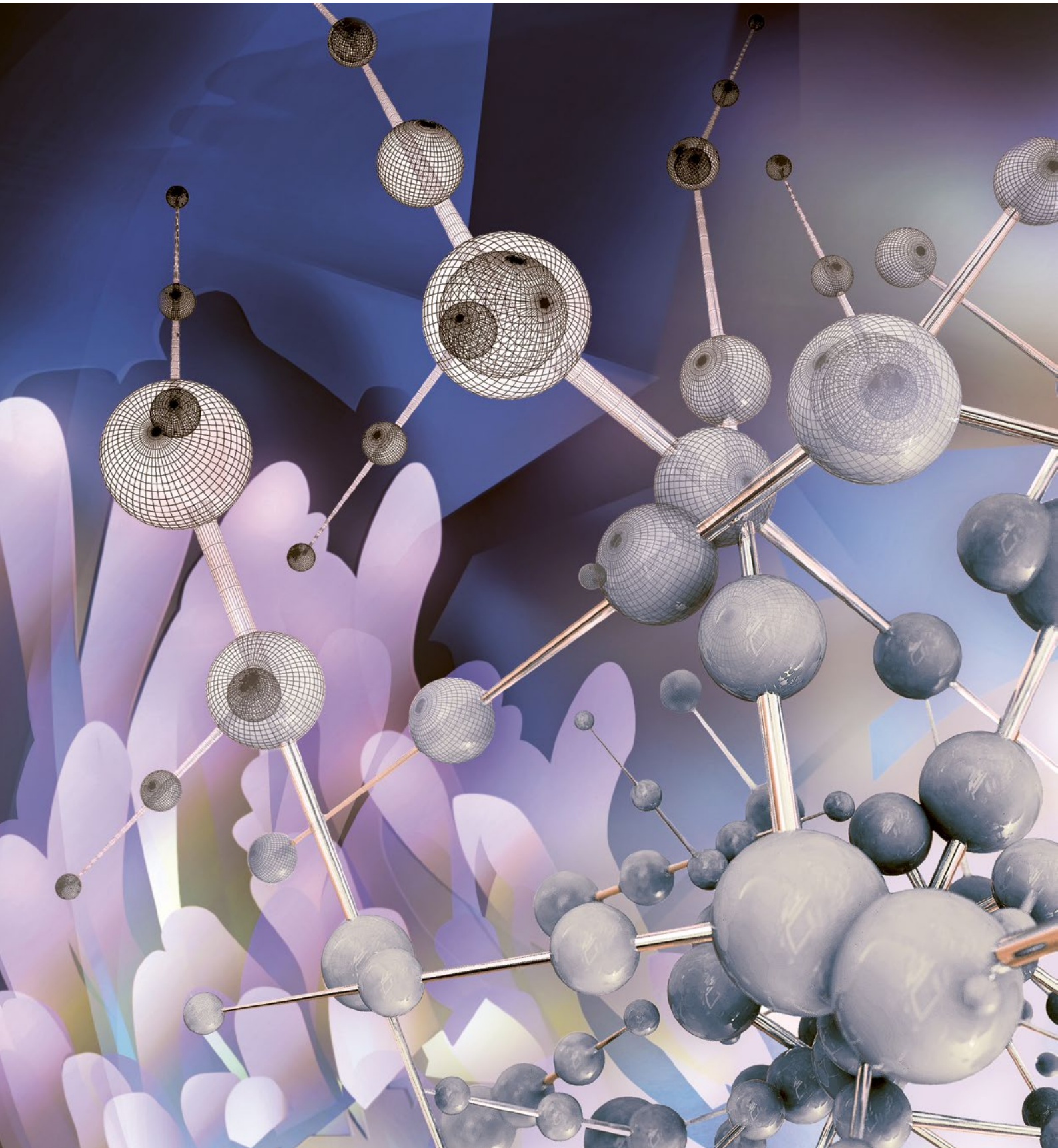
mibelle GROUP biochemistry

SensAmone P5
Immediate comfort for sensitive skin

SWISS QUALITY PRODUCT



SensAmone P5
Immediate comfort for sensitive skin

A Sea Anemone Peptide That is Able to Calm Sensitive Skin
SensAmone P5 is a biomimetic peptide that is based on a sea anemone protein which calms sensitive skin and reduces skin irritation.

Sensitive skin is often characterized by an overactivity of the TRPV1 pain receptor. The result is skin that can react strongly to harmless environmental stimuli with itching or even burning and redness. Therefore, an inhibitor of the TRPV1 receptor could help to calm overreactive skin.

Scientists have recently discovered a unique protein in the venom of the leathery sea anemone that acts as an inhibitor of the TRPV1 receptor.

As the protein is unstable and too large to penetrate the skin, Mibelle Biochemistry has developed a penta-peptide that contains the TRPV1 inhibitor sequence of the sea anemone protein. To ensure improved skin uptake, the peptide was incorporated into a soft sphere carrier system based on shea butter.

An in vitro assay showed that SensAmone P5:
- reduced the activation of the TRPV1 pain receptor
- inhibited TRPV1 in a better manner than the full-length sea anemone protein.

Meanwhile, in clinical studies, SensAmone P5:
- reduced the electrical current perception threshold of the skin, which is an indicator for skin reactivity
- decreased skin sensitivity by reducing the response to skin irritation.

SensAmone P5
- Calms overreactive skin
- Minimizes skin's response to stress
- Reduces the itching sensation of sensitive skin

Applications
- Sensitive skin care
- Neurocosmetics
- Comforting formulations

Formulating with SensAmone P5
- Recommended use level: 1–2 %.
- Incorporation: For cold processes, dissolve SensAmone P5 into the aqueous phase. In hot/cold processes, add during the cooling phase below 40 °C.
- Thermostability: Temperatures of up to 40 °C for a short time will not affect the stability of SensAmone P5.

INCI (EU/PCPC) Declaration
Pentapeptide-59 (and) Hydrogenated Lecithin (and) Butyrospermum Parkii (Shea) Butter (and) Phenethyl Alcohol (and) Ethylhexylglycerin (and) Maltodextrin (and) Aqua/Water

Sensitive Skin
Stressed skin through overactive pain receptors

Environmental Factors Can Lead to Uncomfortable Skin
There are many different types of sensitive skin but the most common type in otherwise healthy individuals is skin that overreacts to environmental factors with irritation. This reaction can range from a feeling of slight discomfort to frequent visible signs of skin irritation, such as redness. Sensitive skin is characterized by an enhanced reactivity to common stimuli – for example, wind, heat, clothes, sunlight and pollution. The result is skin that feels tight, itchy or even has a burning sensation. The main reason for this reaction is a sensory response that is too strong.

The TRPV1 Receptor
The Transient Receptor Potential (TRP) channels play an important role in the transduction of pain from a variety of environmental stimuli. The most important member of the TRP channel family is the TRPV1 vanilloid receptor. This responds to different irritants such as heat, acids and certain chemical compounds by opening up the transmembrane channel to enable the influx of ions into the cell. This in turn leads to the activation of signaling pathways in the cell that ultimately results in an itching or painful sensation.

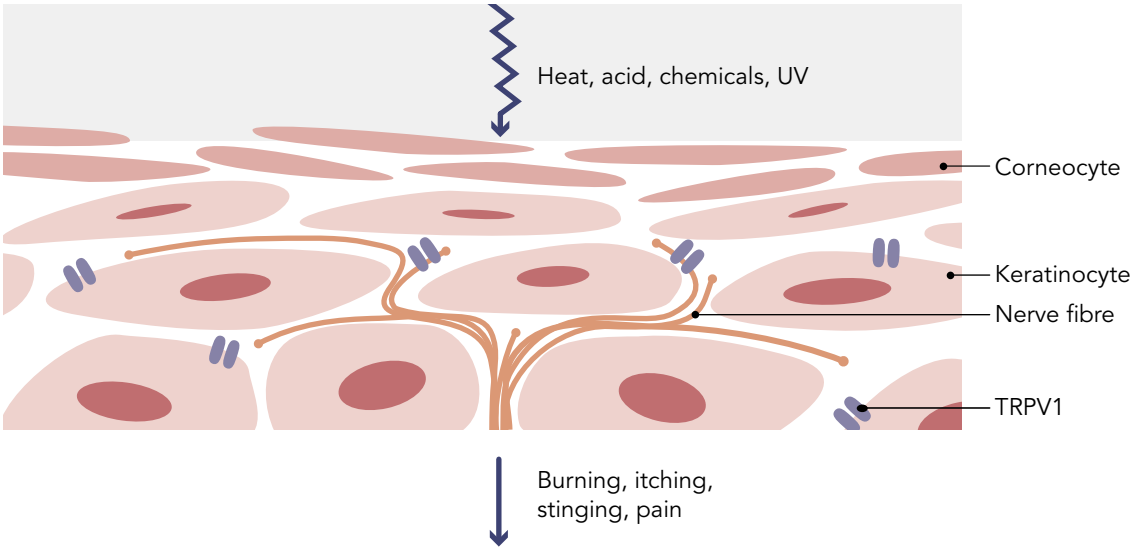
TRPV1 receptors are most common in sensory nerve cells. However, they are also expressed in keratinocytes in the epidermis as these cell types are one of the first to encounter external stimuli and can therefore quickly communicate the pain signal to underlying nerve cells.

The Molecular Cause of Sensitive Skin
An increase of the nerve response to harmless environmental influences is often due to an overreaction of the TRPV1 receptor. This can be the result of a lower activation threshold of TRPV1 as well as higher expression levels of TRPV1 in sensitive skin.

In addition to being responsible for skin discomfort, TRPV1 plays a role in skin aging. In photoaged human skin, TRPV1 is often overexpressed. Furthermore, the constant activation of TRPV1, for example through heat and infrared radiation, leads to the upregulation of enzymes that destroy collagen in the skin and this could result in premature skin aging.

The solution for sensitive skin is to strengthen the tolerance level by reducing the reactivity of TRPV1.

TRPV1 Mechanism



SensAmone P5
A TRPV1 inhibitor peptide from sea anemone

The Leathery Sea Anemone
Heteractis crispa, the leathery sea anemone, inhabits tropical and subtropical waters. It is home to many anemonefish species that use the anemone for shelter. The tentacles of the anemone are armed with cells that contain venom which serves as both a defense mechanism and to capture prey.

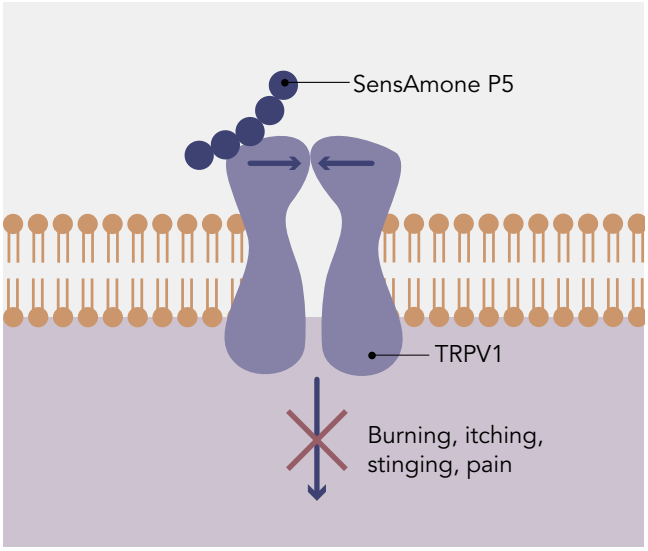
APHC1 – A Special Protein in the Sea Anemone Venom
The venom of the leathery sea anemone consists of proteins and peptides that interact with a variety of cellular targets. Scientists have recently discovered an interesting small protein called APHC1 in the venom of the leathery sea anemone that represented the first polypeptide inhibitor of the TRPV1 receptor*. It was further shown that treatment with APHC1 had ameliorating effects on the pain response in acute and chronic pain models**. This protein is therefore a very interesting molecule for targeting TRPV1 in sensitive skin to reduce irritation.

SensAmone P5 is Designed to Maximize the Calming Capacity of APHC1
In order to render the soothing effect of the sea anemone protein available for cosmetic formulations, a pentapeptide (RRRFV) was designed to model the TRPV1 binding sequence. This was realized in collaboration with scientists at Venomtech (UK) who are experts in venom-based drug discovery.

Furthermore, the pentapeptide was incorporated into a soft sphere carrier system based on shea butter in order to:
- increase its penetration into the skin
- enhance its uptake by skin cells
- enable a controlled-release delivery
- protect the peptide molecules in the formulation against degradation.

*Andreev et al., J Biol Chem, 2008, 283(35): 23914-21
**Andreev et al., Mar. Drugs, 2013, 11: 5100-15

Mechanism of SensAmone P5



SensAmone P5
Study results

Inhibition of the TRPV1 Receptor

The whole-cell patch clamp technique was used to measure the activation of the TRPV1 receptor. By applying this technique, the activation of ion channels in cells can be measured by recording the electrical current change in response to stimuli.

To enable this, a pipette tip is used to clamp onto the cell surface (see the below picture) and the cell membrane is ruptured in that area to allow a free flow of molecules. An electrode is used to detect changes in electrical current.

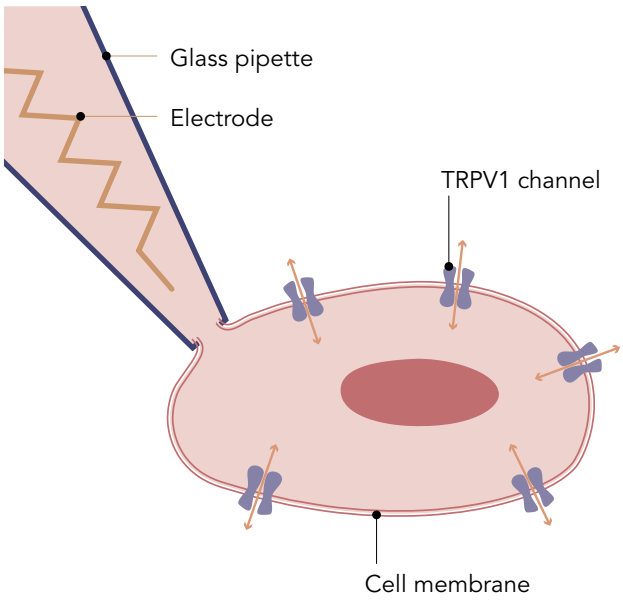
Upon activation, the TRPV1 receptors open channels in the plasma membrane. These channels allow the flow of ions into the cell and therefore change the electrical current that can be measured by the electrode in the attached pipette.

The ability of SensAmone P5 to inhibit the TRPV1 receptor activation was analyzed in CHO cells that express TRPV1 receptors in a stable manner. The cells were irritated with capsaicin, which is an activator of TRPV1, either in the presence or absence of the sea anemone penta-peptide (pentapeptide-59, RRRFV). Treatment with the full-length sea anemone protein APHC1 at the same molecular concentration was used as a positive control.

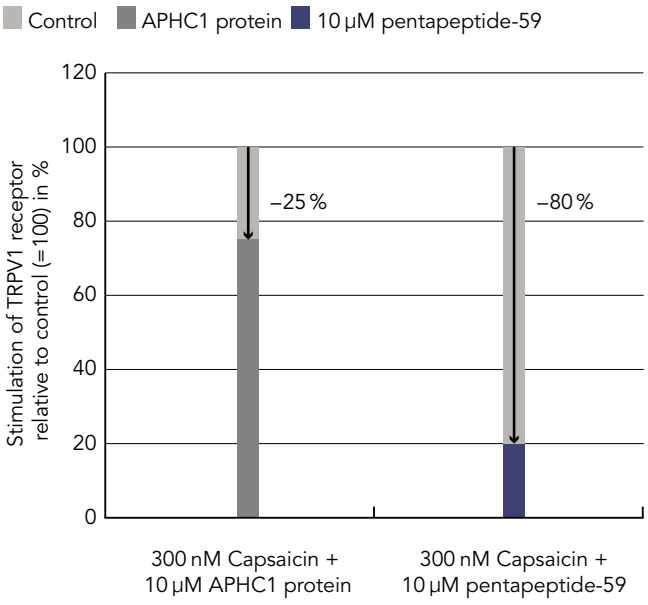
Results showed that treatment with the pentapeptide inhibited TRPV1 receptor activation by 80 %, whereas full-length APHC1 protein inhibited TRPV1 receptor activation by 25 %.

Therefore, the five-amino acid sea anemone peptide exhibits even better TRPV1 inhibition properties than the full-length protein.

Whole-Cell Patch Clamp Technique



Inhibition of TRPV1 Receptor Activation



Instant Reduction of Skin Reactivity following a Single Application

Thirty-one women (mean age: 47 years) with sensitive skin applied a 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.

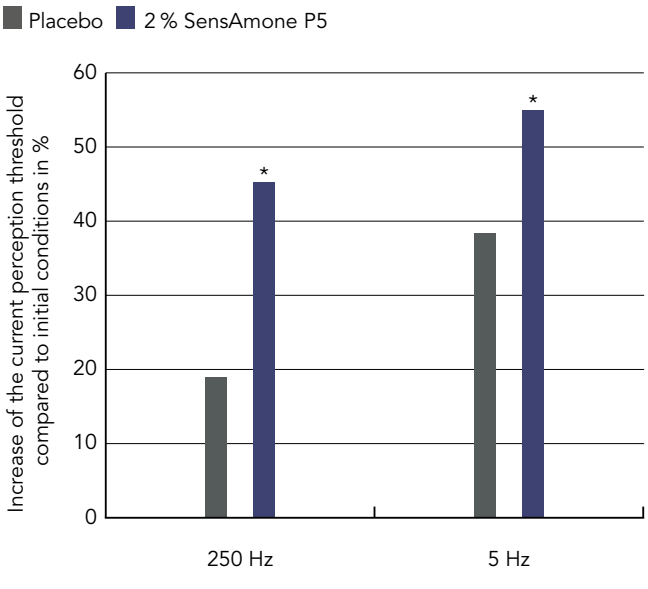
The Neurometer applies an electrical stimulus to the skin at different frequencies in order to target different nerve populations:

- 250 Hz for small myelinated nerve fibers that transmit fast pain, temperature and pressure sensations
- 5 Hz for small, unmyelinated nerve fibers that transmit dull pain and temperature, and are responsible for itching sensations.

The CPT is determined by the amount of electrical stimulus needed for it to be felt by the volunteer. The higher the CPT value, the less reactive is the skin.

A single application of SensAmone P5 significantly increased the CPT of the skin and therefore reduced skin reactivity.

Increase of the CPT after Single Application



*p<0.005 versus initial conditions

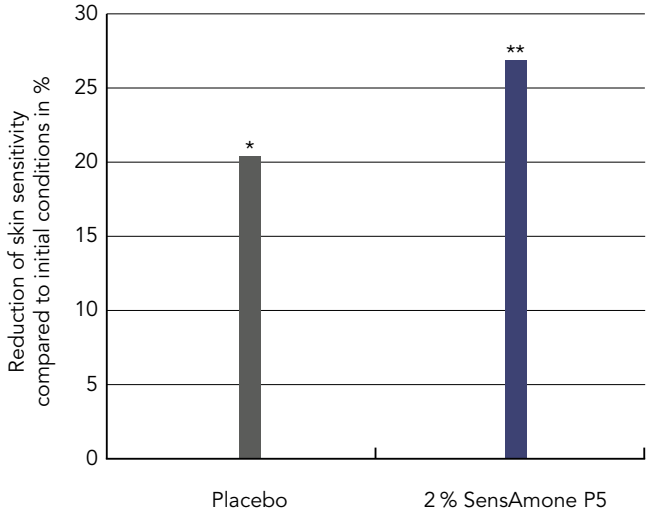
Reduction of Skin Sensitivity

Thirty-one women (mean age: 47 years) with sensitive skin applied a cream with 2 % SensAmone P5 or the corresponding placebo twice daily for a period of 28 days on each side of their face. Skin sensitivity was measured with a lactic acid stinging test. This involved an aqueous 5 % lactic acid solution being applied on the nasolabial fold. The stinging, burning and itching was assessed on a four point scale at one minute intervals for a total period of nine minutes.

Results showed that SensAmone P5 significantly reduced skin sensitivity by more than 26 %.

Therefore, SensAmone P5 can help to protect sensitive skin from overreacting to environmental stimuli.

Reduction of Skin Sensitivity



*p<0.01 versus initial conditions
**p<0.005 versus initial conditions

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Applications
- Sensitive skin care
- Neurocosmetics
- Comforting formulations

Marketing benefits
- Based on venom technology
- Use of a biomimetic peptide
- Neurocosmetics

Innovating for your success
Mibelle Biochemistry designs and develops innovative, high-quality actives based on naturally derived compounds and profound scientific know-how. Inspired by nature – Realized by science.

Mibelle AG Biochemistry, 5033 Buchs / Switzerland, Phone +41 62 836 17 31, info@mibellebiochemistry.com, www.mibellebiochemistry.com