Care Creations™

Skinasensyl™

by Beauty Creations

The neurocosmeceutical soother

BASF
The Chemical Company

Skinasensyl™

New generation cosmeceutical ingredient for sensitive skin

- **Pure tetrapeptide** targeting over-reactive skin by:
- a decrease of the release of pro-inflammatory neuromediators (CGRP),
- a reduction of the response of the sensory nerve fibers to external stimuli, via its binding to the μ-opioid receptor on nerve endings.
- Increase of the **skin's tolerance threshold.**
- **Reduction of sensations of pain and discomfort,** perceived by the end-users.

Sensitive skin

Approximately 40% of the population, of all categories and phototypes, complains of having sensitive skin: they experience sensations of discomfort, tingling, burning and intolerance to certain types of products.

But what is the mechanism hiding behind these symptoms? Which are the causes of sensitive skin? Sensitive skin is healthy but over-responsive, i.e. it will react faster and more intensely to several parameters:
- outside factors: temperature changes, heat as well as cold, sun...
- the use of cosmetic products, certain medicines...

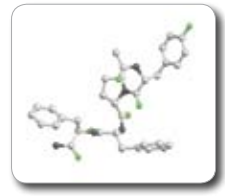
This hyper-reactivity manifests itself through visible and perceivable sensations on the skin, such as redness, burning and itching. These are often temporary, but can develop over several days and may include periodical outbursts.

Sensitive skin is characterized by a lower threshold of tolerance. Currently all of the causes for this are not known yet, but an increase of the permeability of the stratum corneum as well as an exaggeration of the nerve response are considered to be involved in the phenomenon of sensitive skin. Lifestyle has also an effect: tobacco, alcohol, stress, fatigue, emotions...
Sensitive skin is classified in 3 different types based on physiological parameters [1]:
- Type I = low barrier function: alteration of skin barrier function with high TEWL and abnormal desquamation,
- Type II = inflammation: presence of inflammation, but normal barrier function,
- Type III = neurosensitive group: normal barrier function, no inflammation, but exaggeration of the nerve response in the skin.

Although widespread and a clearly complex condition, sensitive skin is not an inevitable fate!
Beauty Creations has developed a pure tetrapeptide based on a new mechanism of action, mainly targeting sensitive skin of group III, able to reduce the nerve response to external stimuli by:
- decreasing the release of pro-inflammatory neuromediators (CGRP: Calcitonin Gene Related Peptide),
- an action mediated via the activation of the μ opioid receptor.

The tolerance threshold of skin is increased, skin is less reactive to different stimuli, and sensations of pain and discomfort are diminished.
This development is especially relevant taking into consideration the growing demand for cosmeceutical products and 'home-use' treatments with effects similar to dermatological procedures, such as microdermabrasion and peels. While becoming increasingly targeted and 'smart', recent skin care products may tend to generate intolerances on very sensitive skin. To allow sensitive skin to benefit from these performing ingredients and treatments without any restriction, it was necessary to develop an active to boost its tolerance... mission accomplished with Skinasensyl™, the first soothing cosmeceutical active which offers sensitive skin the latest advances in cosmetic research.

Definition / Composition



Synthetic acetylated tetrapeptide - Ac-YPFF-NH_2

Skinasensyl™ is a solution of a synthetic acetylated tetrapeptide, N-acetyl-Tyr-Pro-Phe-Phe-NH_2 (Ac-YPFF-NH_2), derived from opioid peptides.
Concentration:
- 470 ppm for the liquid form,
- 1410 ppm for the powder form.

Skin benefits

• Increase of the skin's tolerance threshold.
• Decrease of exaggerated nerve stimulation.
• Reduction of the cutaneous hyper-reactivity to environmental factors and/or to topically applied products.
• Soothing effect to diminish the sensation of discomfort.

Cosmetic use

• Skin care products for sensitive skin.
• Anti-stress skin care products.
• Cosmeceutical ranges.
• Men care products.

Dosage / Solubility / Mode of incorporation

1. Dose of use: Skinasensyl™ LS 9749: 1 - 3%
Skinasensyl™ PW LS 9852: 0.3 - 1%.
2. Solubility: soluble in water, insoluble in oils.
3. Mode of incorporation: Skinasensyl™ LS 9749 is incorporated into the finishing process below 50°C, or at room temperature for cold processing.
Skinasensyl™ PW LS 9852 must be dissolved into 4 times its weight of water heated at 45-50°C, then incorporated into the cosmetic product below 50°C, during the finishing process. It can also be dissolved at room temperature into water for cold processing.
Optimal pH: between pH = 4 and pH = 8

Analytical characteristics

1. Aspect: Skinasensyl™ LS 9749: colorless clear liquid, of weak odor
Skinasensyl™ PW LS 9852: white powder, of weak odor.
2. Specifications: upon request.
3. Preservative: Skinasensyl™ LS 9749: sorbic acid.
Skinasensyl™ PW LS 9852: preservative free.

Tolerance

Good.

Efficacy

Efficacy tests hereafter.

Storage

In its original packaging, at 15 - 25°C.

Regulatory data

INCI name Skinasensyl™ LS 9749:
Water (and) Glycerin (and) Coco-Glucoside (and) Acetyl Tetrapeptide-15
INCI name Skinasensyl™ PW LS 9852:
Mannitol (and) Sodium Citrate (and) Acetyl Tetrapeptide-15

Efficacy tests

The efficacy of Skinasensyl™ to increase the skin's tolerance threshold of neurosensitive skin and its mechanism of action were checked:
- *in vitro*, on the CGRP release from sensory neurons,
- *in vitro*, by a competition test with a μ opioid receptor antagonist on sensory neurons,
- *in vivo*, by measuring the threshold of cutaneous sensitivity to different stimuli: capsaicin and temperature.

CGRP Release From Cultured Sensory Neurons (*in vitro* test) [2]

Aim

Human skin involves many neuritic fibers which allow the central nervous system to be aware of the skin state and outside factors. Activated sensory nerve fibers release proinflammatory neuropeptides such as CGRP and mediate itching, discomfort and pain sensations.

The effect of Ac-YPFF-NH_2 on neuromediator release was evaluated on cultured sensory neurons with or without stimulation by:
- a stinging agent, capsaicin, acting on vanilloid receptor TRPV1,
- a membrane depolarizing agent, KCl.

Capsazepine (antagonist of vanilloid receptors) and verapamil (calcium channel blocker) were used as reference substances.

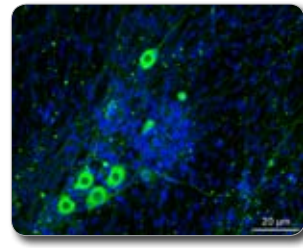


Fig. 1 - Culture of sensory neurons (labeled with anti-β-tubulin ntibody, nuclei stained with Hoechst solution).

Protocol

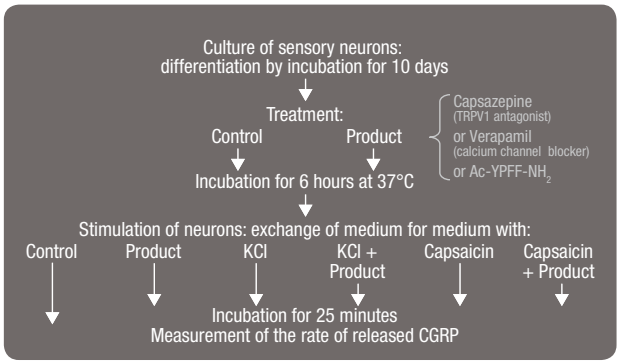
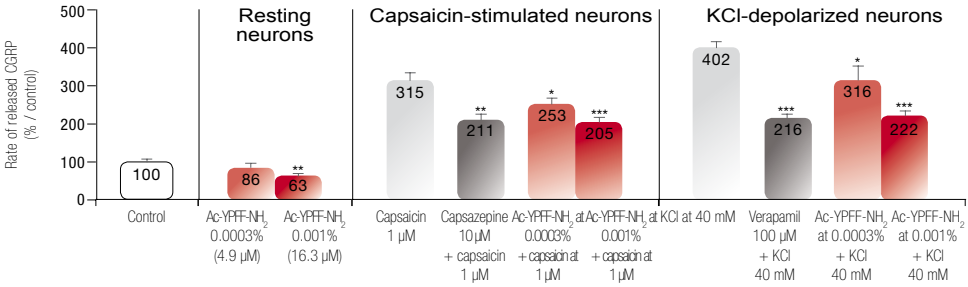


Fig. 2 - Protocol.

Lack of cytotoxicity of the products was preliminary tested on cultured sensory neurons by a MTT test.

Results



Mean ± SEM on 6 replications
Student's t test
(*) $p<0.05$
(**) $p<0.01$
(***) $p<0.001$

Fig. 3- Decrease of CGRP release from cultured sensory neurons.

Conclusion

The tetrapeptide Ac-YPFF-NH_2 (active matter of Skinasensyl™) has significantly reduced the neuronal release of neuromediators. These results show the potential of Skinasensyl™ to appease neuronal hyper-reactivity to environmental stimuli.

Mechanism of action (*in vitro* test)

Aim

To validate the action of Ac-YPFF-NH_2 via μ opioid receptor, a competition test has been conducted between the peptide and naloxone (opioid receptor antagonist) on cultured sensory neurons after capsaicin stimulation.

Protocol

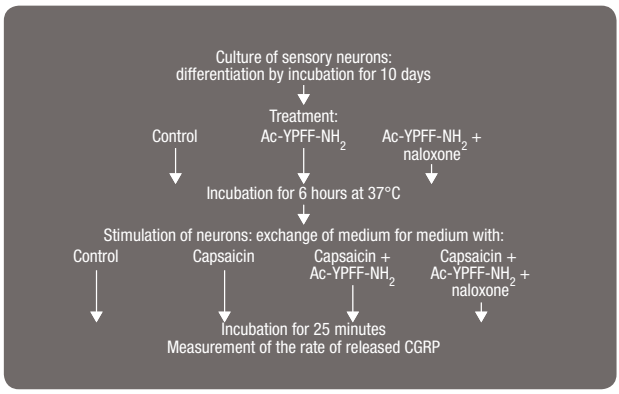


Fig. 4 - Protocol.

Results

Ac-YPFF-NH_2 has decreased the rate of released CGRP in capsaicin-stimulated neurons, but this effect was abrogated in presence of the opioid receptor antagonist, naloxone. These results show that the inhibitory effect of Ac-YPFF-NH_2 on the capsaicin-induced CGRP release is mediated via binding on the μ opioid receptor. The signal pathway involved goes through the inhibition of adenylate cyclase (ADC) to inhibit cAMP-dependent PKA which potentiates the TRPV1 response (figure 6) [3].

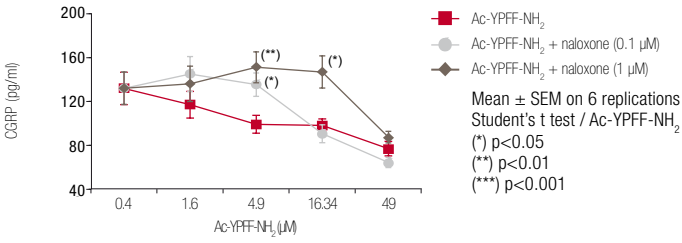


Fig. 5 - Competition between Ac-YPFF-NH_2 and the opioid antagonist naloxone on CGRP release by sensory neurons after capsaicin stimulation.

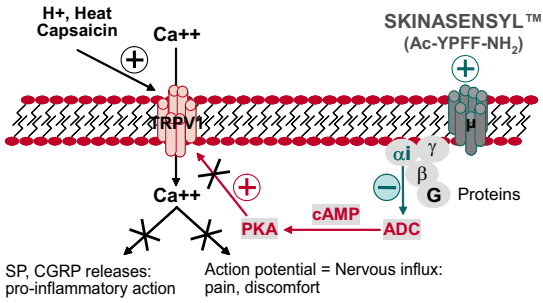


Fig. 6 - Inhibitory action of Ac-YPFF-NH_2 on capsaicin-evoked TRPV1 response via the μ opioid receptor.

Conclusion

The tetrapeptide Ac-YPFF-NH_2 (active matter of Skinasensyl™) attenuates the neuronal stimulation via binding on the μ opioid receptor.

Soothing effect: cutaneous capsaicin sensitivity (clinical test)

Aim

Cutaneous application of capsaicin stimulates nerve endings and causes the appearance of uncomfortable sensations such as itching, burning or stinging. The prevention of these sensations on the skin has been evaluated by determinating the detection threshold to increasing concentrations of capsaicin [4] before and after 4 days of treatment with Skinasensyl™.

Protocol

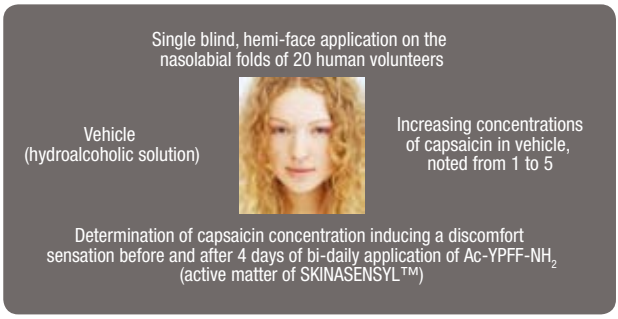


Fig. 7 - Protocol.

Results

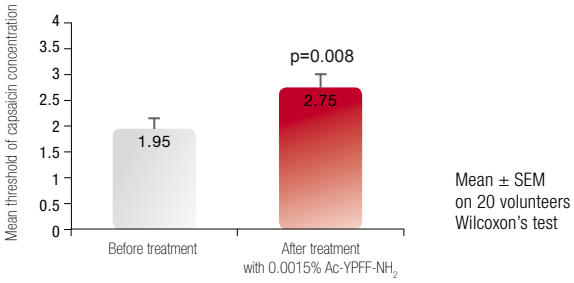


Fig. 8 - Increase of perception threshold after treatment with Ac-YPFF-NH_2 at 0.0015% (i.e. 3% Skinasensyl™) in hydroalcoholic solution / capsaicin stimulus.

Conclusion

The tetrapeptide Ac-YPFF-NH_2 (active matter of Skinasensyl™) has significantly increased the threshold of capsaicin concentration which provokes uncomfortable sensations. The soothing activity is achieved by prevention of itching, stinging.

Bibliography

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Soothing effect: cutaneous thermal sensitivity (clinical test) [5]

Aim

The heat perception involves sensitive anatomical elements such as corpuscles and receptors on free terminal nerve fibers. The soothing effect on the skin has been evaluated by measuring the Cutaneous Thermal Sensitivity (CTS), using a thermal probe applied on the skin.

Protocol

16 human volunteers
Single randomized application on the back for an immediate effect

Placebo emulsion

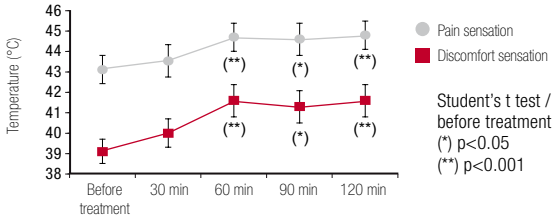
Emulsion with 2% SKINASENSYL™ (i.e. 0.001% Ac-YPFF-NH_2)

Evaluation of discomfort and pain sensations, using a thermal probe before and up to 120 minutes after application

Fig. 9 - Protocol.

Results

A: increase of perception threshold with time after treatment with 2% Skinasensyl™



B: difference of perception threshold after treatment with emulsion with 2% Skinasensyl™ and placebo emulsion

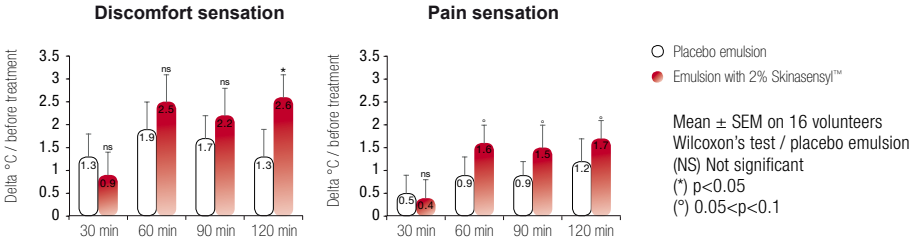


Fig. 10 - Increase of perception threshold after treatment with Skinasensyl™ at 2% in an emulsion / thermal stimulus.

Conclusion

Skinasensyl™ at 2% helps to relieve sensitive skin by a reduction of the cutaneous over-reactivity. The tolerance threshold of the skin is increased, the skin is less reactive and sensations of pain and discomfort are diminished.

General conclusion

Thanks to the capacity of Skinasensyl™ to reduce the release of CGRP from sensory nerve endings, via its demonstrated mechanism of action on the μ opioid receptor, over-reactive skin can recover the right to comfort. Two clinical studies with different stimuli have confirmed that Skinasensyl™ has a strong ability to increase the skin tolerance threshold, skin is less reactive. The main complaints of sensitive skin such as sensation of discomfort and pain are perceivably reduced. This prevention of unpleasant sensations can be extended to other kinds of stimuli also known to induce neuron stimulation. With the performing activity of Skinasensyl™, sensitive skin is significantly soothed, and can be offered all the latest skin care treatments without concern.

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