Active Beauty

Sensityl™

The sensitive skin good mood influencer

Crafted by blue technology

Givaudan

engage your senses

Focus on the product

Happy skin, happy mood?

Skin and brain share the same origin and there is indeed an entire branch of the peripheral nervous system in the dermis and epidermis. This constant communication is a legacy of our adaptation[1]. The skin interfaces with the brain, as an external sensor for all the stress that we receive. **This brain-skin axis** enables an efficient management of our reaction to stress and all of the consequences of our mood and emotions, specifically in continuous skin stress conditions.

Stress factors which affect the skin induce a whole cascade of reactions in dermal and epidermal nerves systems, as well as nerve endings, mast cells and immune cells.

Skin sensitivity (also called "itchy skin", "reactive skin","skin discomfort", "tight skin feeling)" is a typical condition in which a set of stress factors triggers a cascade of biological reactions[2], which ultimately **impacts our mood, influences our self-confidence and increases our difficulties in a social context** due to this persistent negative skin feeling.

Sensitive skin: from microbiota balance to wellbeing impact

The main causes of sensitive skin are genetic predispositions, hormonal factors, ageing and exogenous factors[3]. Sensitive skins are subject to an altered barrier function, allowing penetration of various substances and opportunistic pathogens thus leading to the immune system activation and recruitment of immune cells. Then the cytokines release will lead to visible inflammation, redness, and ultimately sensations of twinging and itching.

It is now established that the skin microbiota also has an impact on the skin sensitivity status[4] by triggering skin immune system. Typically, a loss of microbiota diversity is observed in skin conditions related to sensitivity[5].

On the long term, sensitive skins are subject to "inflamm'ageing". This process starts when the skin is suffering from a **chronic inflammation**[6] and leads to an exhausted defence system that will **affect not only our skin, but our wellness as well**, as low-grade inflammation is recognised as a main characteristic of ageing bodies.

Sensityl™: forget about skin discomfort, enhance your mood!

Sensityl™ is a **natural extract** obtained from the most active compounds of ***Phaeodactylum tricornutum***, thanks to a bio-guided evaluation combined with a metabolic profiling. Coming from the dominant class of marine phytoplankton, diatoms, this microalgae is found in coastal marine or brackish waters in temperate zones.

Sensityl™ offers soothing and calming actions to the skin by rebalancing sensitive skin microbiota and taking control over the whole inflammation process.

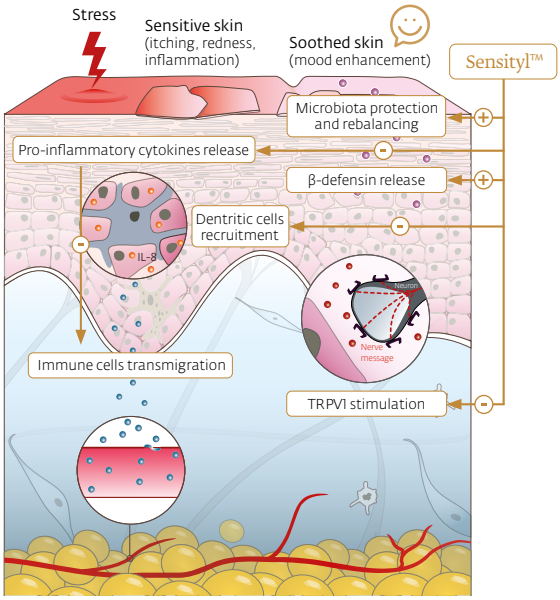
Acting through microbiome, epigenetic & genetic regulation, Sensityl™ acts on:

- rebalancing and protecting skin microbiota,
- reducing the immune cell recruitment,
- reducing the pro-inflammatory mediators (IL-8),
- decreasing the pain sensation (TRPV1),
- increasing the anti-microbial defences of the skin.

Sensityl™ reduces redness and soothes the skin, but even more, it helps to enhance consumers' mood.

Active Beauty has leveraged two innovative non-verbal methods, for the 1st time in the cosmetics industry, **to understand consumers' emotional responses** while overcoming the barrier of using words.

Forget about skin discomfort, and feel good again!



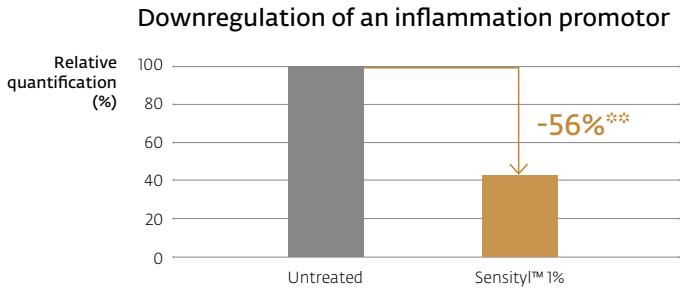
[1] D. B. Yarosh et al. 2016 [2] E. Berardesca et al. 2012 [3] T. Yatagai et al. 2017 [4] Seite et al. 2018 [5] Dreno et al. 2017 [6] Franceschi et al. 2000

Biological activity

Epigenetic control of inflammation through exosomal communication (*in vitro*)

Keratinocytes were treated with Sensityl™ at 1% directly in culture medium for 24 hours. Exosomes from keratinocytes supernatants were then applied as treatment in a fibroblasts culture for 24 hours. miRNA quantification from fibroblasts was done using RT-qPCR. The targeted miRNA, mir-21, has been demonstrated to be an "inflamm-miR", promotor of inflammation[1].

Results: Sensityl™ **protects the skin from inflammation by epigenetic control through exosomal communication**.



Student's t-test: ** p<0.01

Genetic control of skin soothing and calming (*in vitro*)

Cellular function	Proteins name	Fold expression
Anti-inflammatory	IL1-α - Interleukin-1 Alpha	-1.37***
	SPP1 - Secreted Phosphoprotein 1	-1.78*
	LTB4R2 - Leukotriene B4 Receptor 2	-1.29**
	CALM1 - Calmodulin 1	-1.48***
Skin calming	NGFR - Nerve growth factor receptor	-2.14***
	RAMP1 - Receptor activity-modifying protein	-1.29**
	CALCRL - Calcitonin gene-related peptide type 1 receptor	-1.44**
	TRPV1 - Transient receptor potential cation channel subfamily V member 1 (Capsaicin receptor)	-1.41*

Student's t-test: *p< 0.05, **p< 0.01, ***p< 0.001

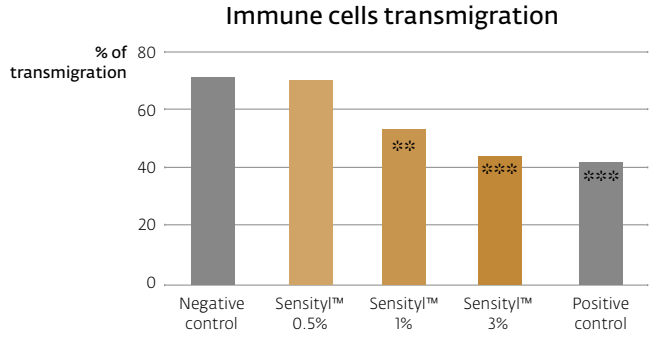
A transcriptomic analysis was performed on normal human keratinocytes on which product was applied at 3% for 18 hours. The mRNA expression of genes was quantified by RT-qPCR.

Results: Sensityl™ significantly **downregulates a complete set of genes involved in anti-inflammatory & soothing activities.**

Control of the acute phase of inflammation

1. Inhibition of immune cells transmigration (*in vitro*)

Human umbilical vein endothelial cells (HUVECs) were treated after cultivation for 10 hours with TNF-α (500 U/mL) and different concentrations of Sensityl™ or a positive control (M1/70 antibody). Monocytes were collected from healthy donors. These monocytes suspension was then flowed over a HUVECs monolayer, and images of the captured monocytes were taken using phase-contrast microscopy, and a high-resolution camera, in order to quantify adherent monocytes. Adhesion events were recorded as the total number of cells per unit field (mm²). Transmigration events were then presented as a percentage of total monocytes.



Student's t-test *vs* negative control: **p<0.01, ***p<0.001

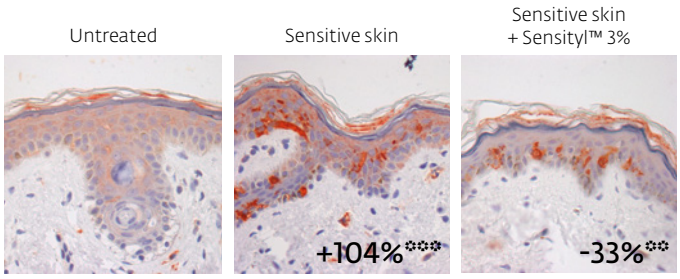
Results: An increasing concentration of Sensityl™ reduces the transmigration of monocytes in a dose dependent effect. Sensityl™ here **demonstrates an anti-inflammatory effect by reducing immune cells (monocytes) recruitment.**

[1] Shijin Xia et al. 2016

Biological activity

2. Inhibition of immune cells recruitment (*ex vivo*)

Human skin explants from 3 donors (33, 52, 44 years old) were preventively treated topically with Sensityl™ at 3%, 2 hours before application of a sensitive skin model (one topical application of 15 µL/cm² of 1% SLS for 1 hour, followed by a rinse (PBS) then addition of 5µM capsaïcin in the culture medium), and exposure to UVB (2 J/ cm²) after 2 hours, to boost the reactivity of the skin. Skin explants were then kept in survival for 24 hours. Immunodetection was then performed to label dendritic cells (immune cells), showing a +104% increase in the sensitive skin model.



Student's t-test *vs* untreated: ***p<0.001, Student's t-test *vs* sensitive skin: **p<0.01

Results: Sensityl™ at 3% **protects sensitive skin by significantly reducing the number of dendritic cells** (immune cells), down to -33% compared to the sensitive skin.

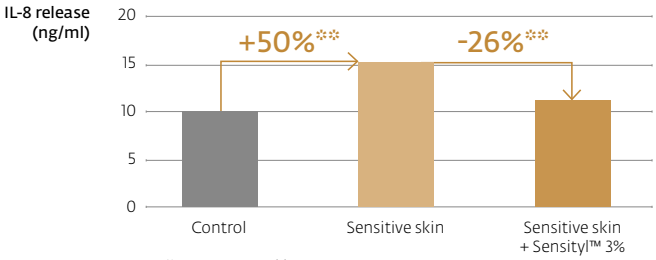
Control of inflammatory cytokines and pain receptors (*ex vivo*)

The following 2 tests were performed on the same skin explants and with the same protocol than the previous test.

1. Reduction of pro-inflammatory signal through IL-8 inhibition

The assay of IL-8, pro-inflammatory cytokine (ng/ml) was performed from culture media by an immunoassay technique with spectrophotometric reading. A significant increase of 50% in the IL-8 release was observed in the sensitive skin compared to the control skin.

Results: Sensityl™ at 3% **reduces inflammatory response by significantly reducing the level of IL-8**, down to -26% compared to the sensitive skin.

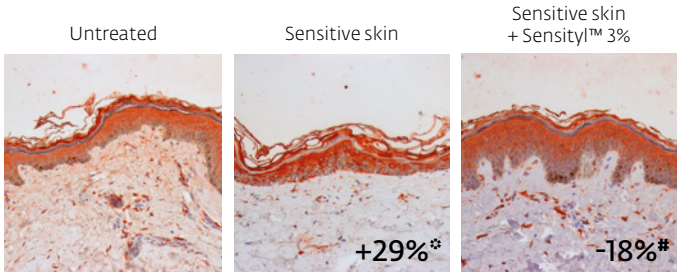


Wilcoxon test: **p<0.01

2. Reduction of pain sensation through TRPV1 expression reduction

TRPV1 receptors were highlighted in the epidermis. The immuno detection was made with an indirect technique of immunperoxydase. A significant increase of 29% in the expression of TRPV1 was observed in the sensitive skin compared to the control skin (red marker in the pictures beside).

Results: Sensityl™ at 3% **inhibits TRPV1 receptors, responsible for pain, twinge and itching sensations**, down to -18% compared to sensitive skin.

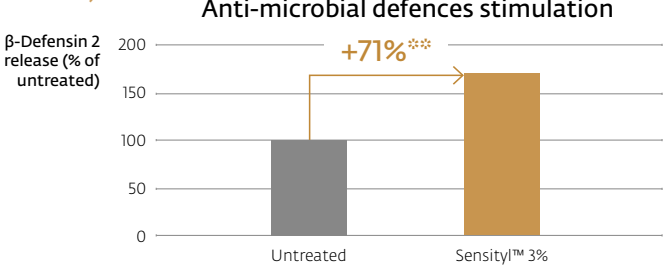


Student's t-test *vs* untreated: *p<0.05, Student's t-test *vs* sensitive skin: #p<0.1

Control of microbial proliferation (*ex vivo*)

Human skin explants from 3 different donors (55, 60, 66 years old) were left untreated or treated topically twice a day for 3 days with Sensityl™ at 3%. Culture medium was then collected on day 3 on the evening and β-Defensin 2 (antimicrobial peptides) were quantified through ELISA assay.

Results: Sensityl™ **demonstrates its anti-microbial properties to protect the skin by increasing the β-Defensin 2 release**, up to +71%.



Student's t-test: **p<0.01

Efficacy

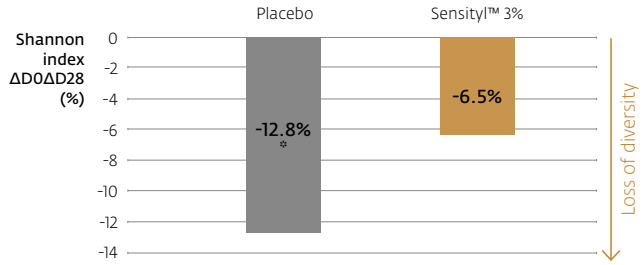
Protection of skin microbiota against sensitive skin conditions (clinical test)

A double blind and placebo controlled study was performed on 41 volunteers (average age of 39 years old), recruited for their sensitive skin. 2 groups had to apply on their face a formula either containing Sensityl™ at 3% or a placebo, twice a day for 28 days. A microbiome clinical study (16S rRNA) was performed at D0 and D28 by swabbing volunteers' cheeks, then extracting and sequencing the 16S rRNA gene (V3V4 region) of the collected microbiomes. 11.3 billions of DNA bases were analysed to compare the evolution of the microflora composition over time under the two conditions.

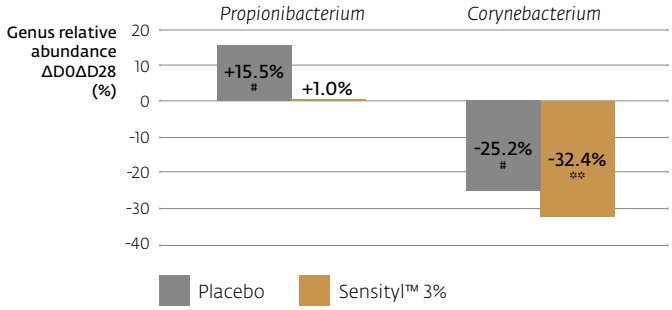
Results: Sensityl™ **protects the diversity of skin microbiota**, a key factor which can be linked to various inflammatory skin conditions when impacted[1]: no significant modification of diversity is observed at D28, while the placebo decreases it drastically. Additionally, Sensityl™ **improves the microbiota composition**, by stabilising *Propionibacterium* (now known as *Cutibacterium*) and significantly decreasing *Corynebacterium* populations, both of which having been linked to proinflammatory features[2].

Sensityl™ **acts on the skin microbiota to protect and improve its composition, rebalancing its equilibrium from sensitive skin to normal skin conditions.**

Microbiota diversity protection



Microbiota composition improvement



Wilcoxon test: # p<0.1, * p<0.05, ** p<0.01

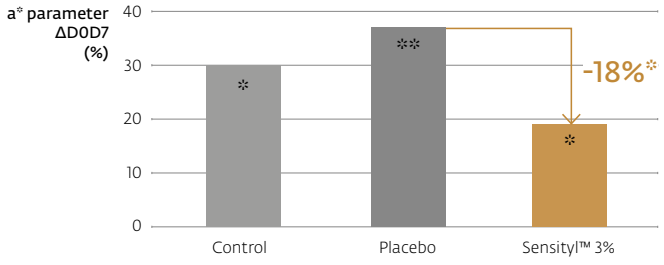
Restoration and protection of sensitive skin (clinical test)

1. Skin irritation reduction in just 7 days

A double blind and placebo controlled study was performed on the forearms of 20 volunteers (average of 46 years old) to measure the anti-irritation activity of Sensityl™. After application of a SLS patch at 10% for 24 hours, a cream containing Sensityl™ at 3% or a placebo was applied twice a day during 7 days. The colour of the skin was then measured thanks to a spectrocolorimeter (a* parameter).

Results: Sensityl™ at 3% significantly **reduces the skin irritation**, down to -18% *versus* placebo, with a visible effect on 100% of the volunteers.

Skin irritation reduction



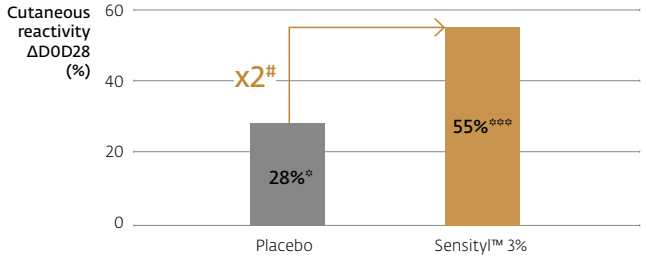
Wilcoxon test: * p<0.05, ** p<0.01

2. Improvement of cutaneous reactivity

A double blind and placebo controlled study was performed on 41 volunteers (average age of 39 years old), recruited for their sensitive skin. 2 groups had to apply on their face a formula either containing Sensityl™ at 3% or a placebo, twice a day for 28 days. At D0 and D28, capsaicin was applied on the nasolabial fold to perform a stinging test.

Results: Sensityl™ at 3% **enables a significant improvement of the skin reactivity,** up to 2 times more efficiently than the placebo.

Cutaneous reactivity improvement



Mann Whitney test: # p<0.1, * p<0.05, *** p<0.001

[1] Dreno et al. 2017 [2] SanMiguel et Grice 2015, Ridaura et al. 2018, Ray et al. 2015, Ma et al. 2018

Efficacy

A soothed skin for a better mood (clinical neuroscience)

1. Mood Portraits®: a non-verbal method

Mood Portraits® is a unique non-verbal neuroscience method, developed by Givaudan[1], using pictures to measure consumers' mood and emotional responses to various stimuli. This test follows our clinical study on 41 volunteers during 28 days (same panel than microbiome clinical study). All participants completed the method on Day 0 (baseline) and Day 28. During this study they were asked to answer one question at D0 and D28, by selecting pictures randomly displayed on a wall in front of them:

"Thinking about your skin, how do you feel about it now? Please pick all the pictures that reflect your feelings."

Based on their pictures selection, our neuroscience experts are able to analyse the main moods expressed by the participants.

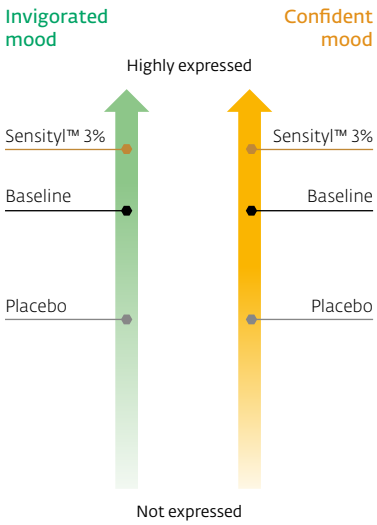
Results:

Baseline D0

Sensityl™ D28

Positive vibes

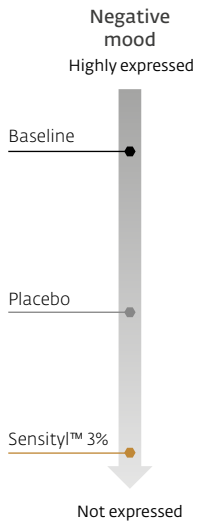
After a month, **confident** and **invigorated** moods are significantly expressed only among the Sensityl™ group (not expressed in the placebo group).



Additionally (not shown on graph), **refreshed** and **relaxing** moods are expressed in both groups, but with higher scores for Sensityl™.

6% *versus* 50%

After a month, the **negative mood** is significantly reduced thanks to Sensityl™.



Only 6% of the volunteers in the active group selected negative pictures, *versus* 50% at D0.

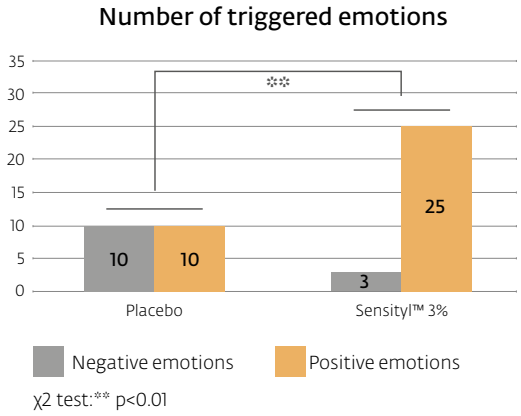
[1] A. Churchill et al., 2010

Efficacy

2. Emotion Decoding System®: evaluating the unconscious emotions

An expert PhD in non-verbal communication used a unique grid to analyse over 200 non verbal reactions (facial reactions, postures, gestures, voice), and remove all verbalisation barriers[1].

This test follows our microbiome clinical study and was carried out on 40 volunteers during 28 days. The purpose of this test was to measure the impact of a soothing facial cream containing Sensityl™ or a placebo on consumers' emotions.



χ2 test:** p<0.01

Sensityl™ is very effective emotionally, as it provokes a significantly higher number of positive emotions and significantly lower number of negative emotions than the placebo. Additionnally, it has generated a wider range of positive emotions: **sensuality, protection, happiness, appeasement, fortitude**.

Sensityl™ 3%

Happiness

- Opening of the eyes
- Raised eyebrows
- Laugh

Sensuality

- Caressing her face / hair
- Rubbing fingers to evoke a soft texture

Protection + Apeasement

- Shrug
- Hands encompass to simulate the protected body

Placebo

Contrariety

- Tilt the head to one side
- Pouting on the mouth
- Grinning

Unpleasantness

- Frowned eyebrows
- No with the head

Disinterest

- Pouting of the mouth
- Shrug

[1]Work of Marina CAVASSILAS, PhD in Linguistic, based on work from US psychologist P. Ekman, demonstrating that emotions drive non-verbal reactions, in a universal way.

Summary

Technical information

INCI:	Water (and) Phaeodactylum Tricornutum Extract (and) Pentylene Glycol
Origin:	Marine biotechnology
Preservation:	Sodium Benzoate (and) Benzoic Acid
Appearance:	Clear yellow liquid
Solubility:	Water soluble
Dosage:	1-3%
Processing:	Can be added to the water phase at the end of the formulation process, at a pH between 2 and 7.

Claims

Claims:	Soothing, calming, neuro-soothing, indirect mood enhancer (through skin calming), skin reactivity inhibitor, sensitive skin pacifying, skin microflora rebalancing, protecting and enhancing skin microbiota composition.
Applications:	Every day cream for sensitive skin, feel-good cream, healthy glow lotion, cold cream, after-sun, shampoo, post-epilatory, post-peeling, after-shave.

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