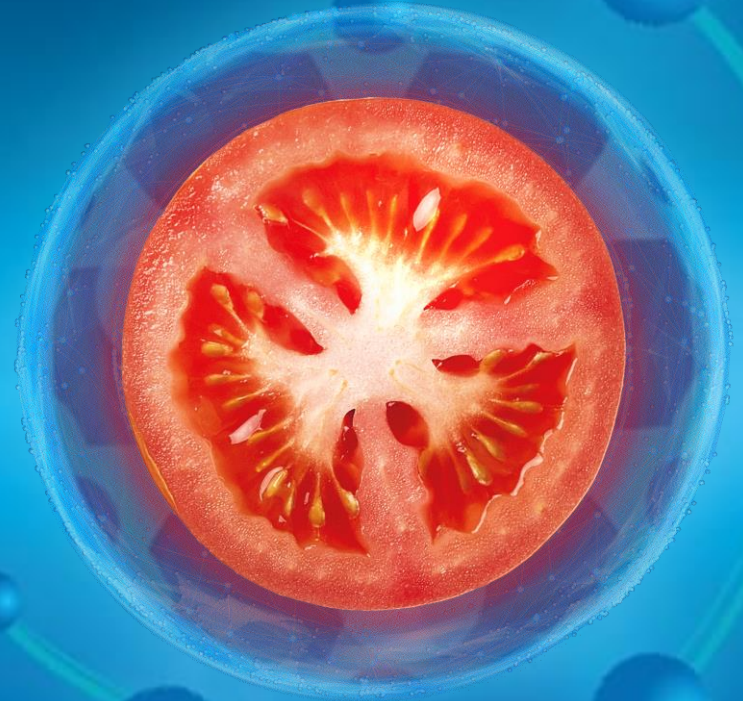


INTELLIGENE® RANGE

SENSITIVE SKIN / HOMEOSTASIS

**Phenix**®
en Provence



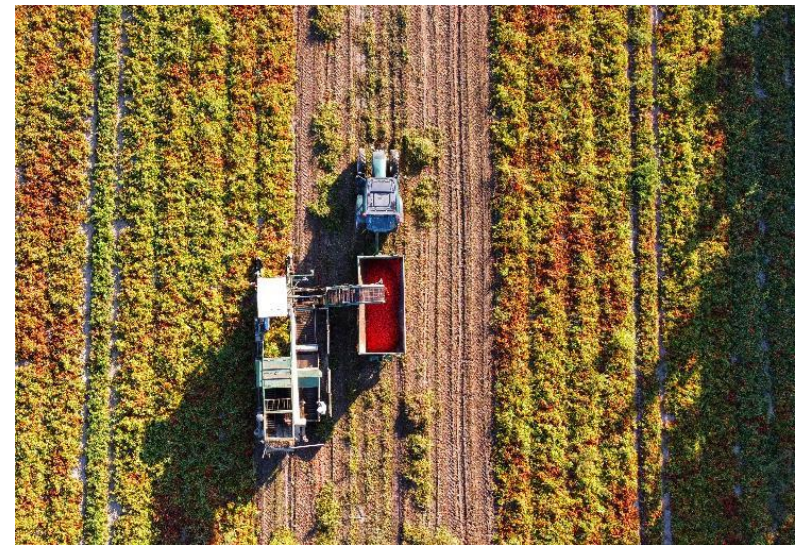
“ BEAUTY OF THE FUTURE ”

**Sollice**
BIOTECH



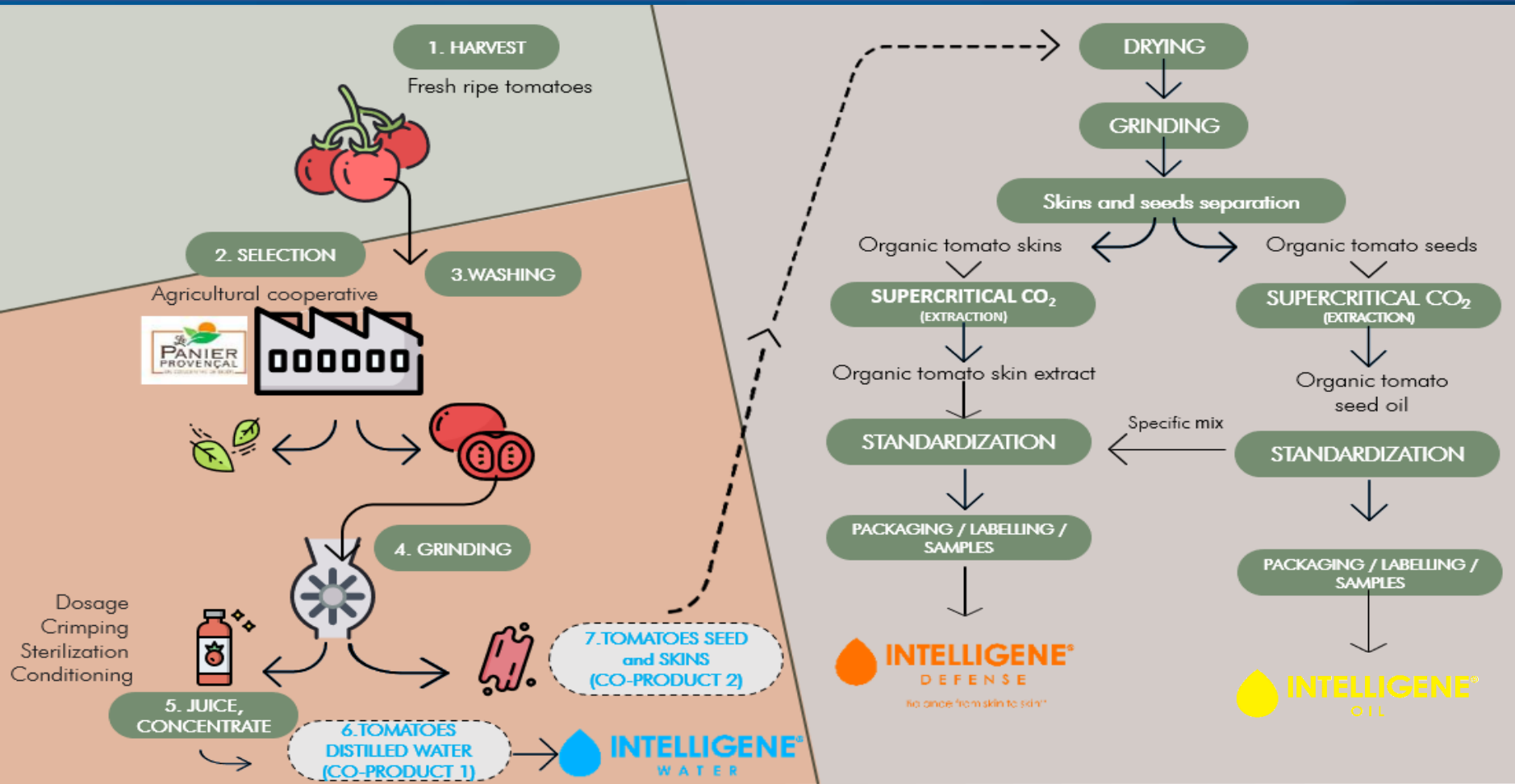
ORIGIN

- In France, 160 000 T of tomatoes are produced in **Provence** where 14 000T are from **organic** farms (~80% of total organic French tomatoes).
- **Phenix en Provence** is a Joint-Venture between Inaturals and CAPL (Coopérative Agricole de Provence et Languedoc) that is producing and commercializing **INTELLIGENE® range, cosmetic ingredients** obtained from organic tomatoes co-products.
- It is an **exclusive** association between an R&D independent office and French farmers, promoting **science and a local and circular economy**.





FABRICATION PROCESS





INTELLIGENE INGREDIENTS

- The **INTELLIGENE**[®] range allows the skin to restore its balance, hydration and radiance
- 1 active ingredient
- 2 commodities



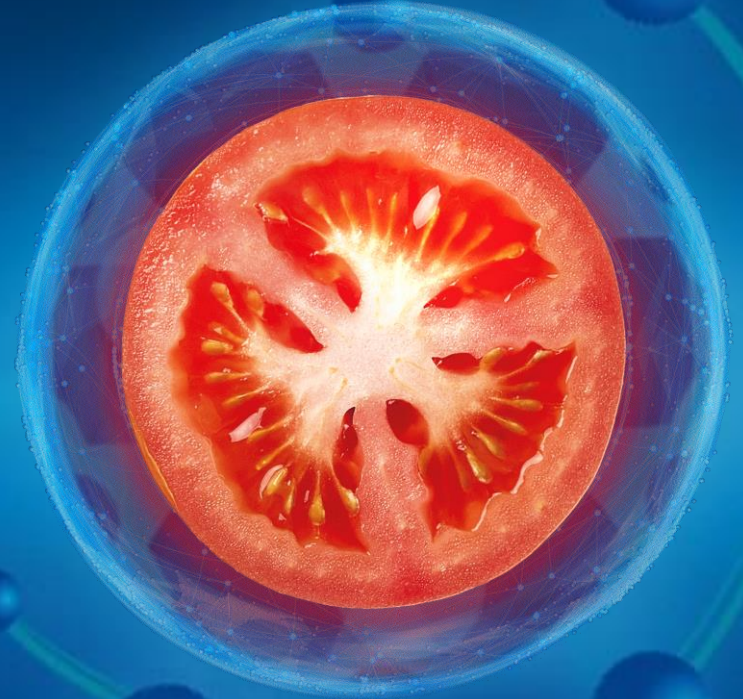
INTELLIGENE® RANGE

SENSITIVE SKIN / HOMEOSTASIS



INTELLIGENE® DEFENSE

Balance from skin to skin™



“ BEAUTY OF THE FUTURE ”

UNIQUE COMPOSITION

- A **unique wax** from tomato skin, depleted in lycopene and carotene.
- Contains **triterpenoids**, polycyclic compounds derived from the linear hydrocarbon squalene, with multiple biological activities.

Amyrins dedicated to tomato defense

Compounds	(%, by HPLC-MS)
Amyrins	~1.5
Oleic acid	~15
Linoleic acid	~45
Lycopene + β -caroten	<0.3

PATENTED
Ongoing



NECESSARY DEFENSE

EXPOSOME

External factors

meteorological factors, solar radiation, pollution or tobacco smoke, cosmetics...

Internal factors

unhealthy diet, hormonal variations, lack of sleep, psychosocial stress...

Clinical manifestations

- Sensitive skin
- Premature skin aging
- Dry skin, accentuate fine lines
- Pruritus, erythema
- Pale skin
- Flares of inflammatory skin conditions such as acne, rosacea, atopic dermatitis, pigmentation disorders



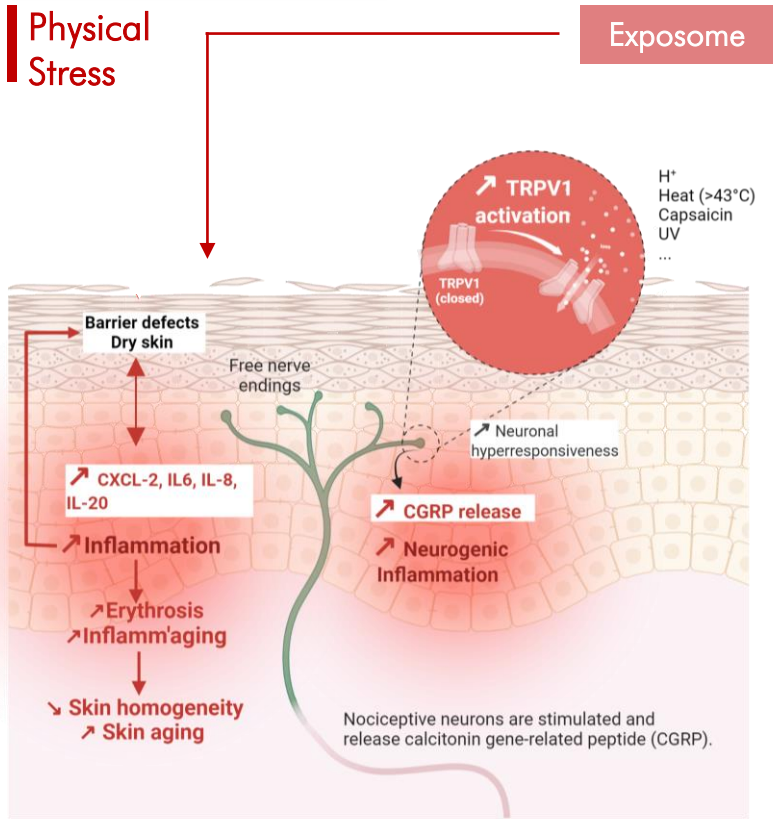
60% OF
PEOPLE

Passeron T, *et al.* J Eur Acad Dermatol Venereol. 2021
Misery L, *et al.* Acta Derm Venereol. 2017

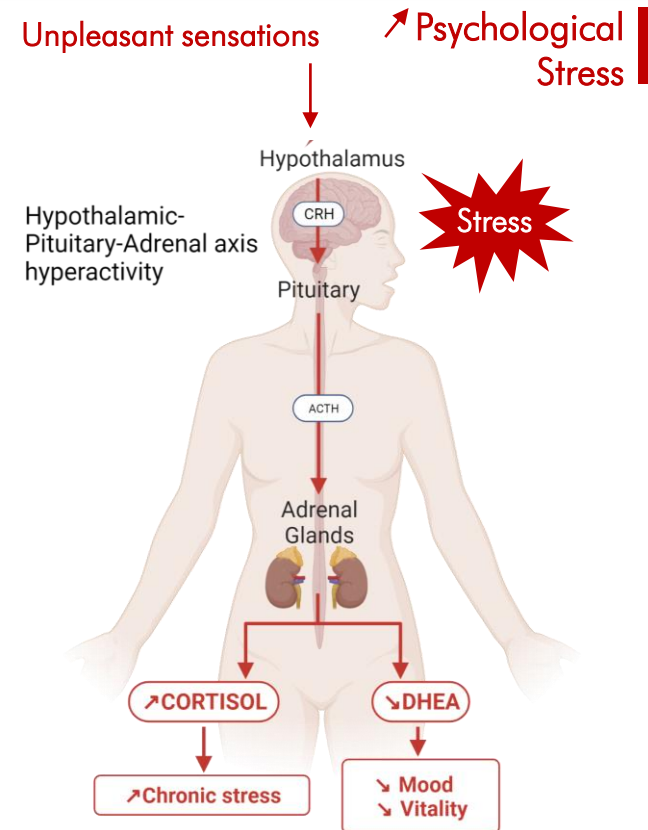
MECHANISM OF ACTION

A systemic approach of sensitive skin

BIOLOGICAL



PSYCHONEUROENDOCRINOLOGICAL





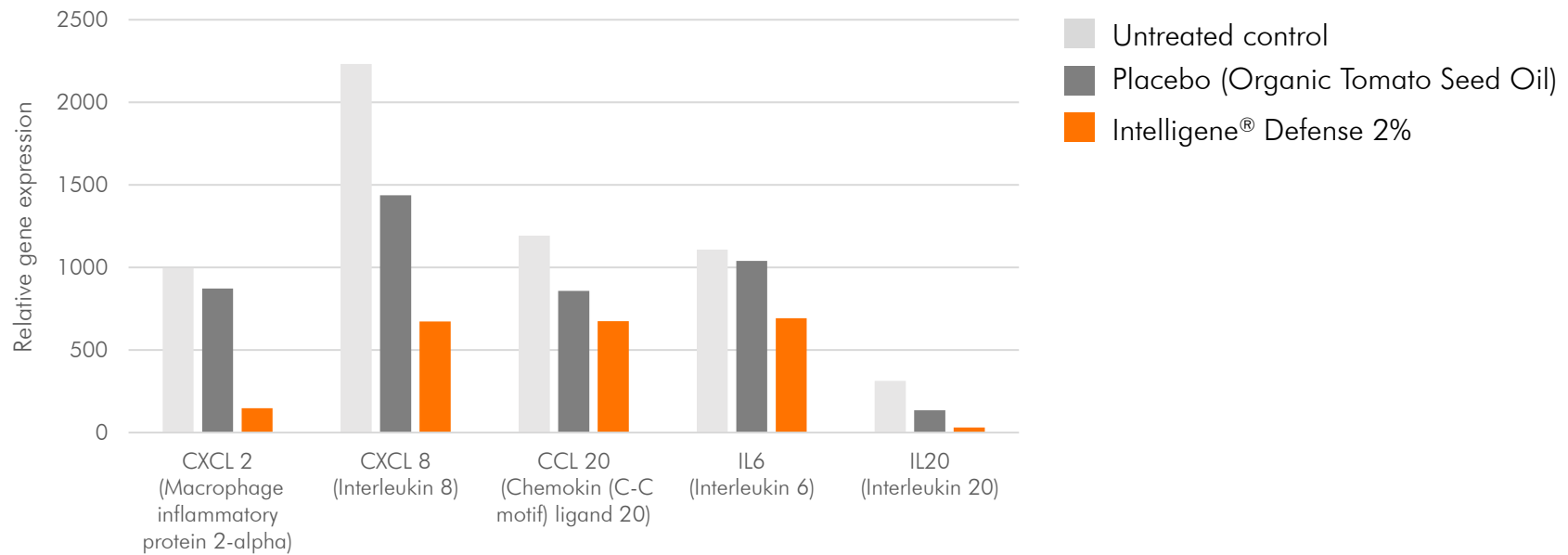
BIOLOGICAL MECHANISM





REGULATES INFLAMMATORY RESPONSE

INTELLIGENE® DEFENSE inhibits the expression of key genes involved in inflammatory response.

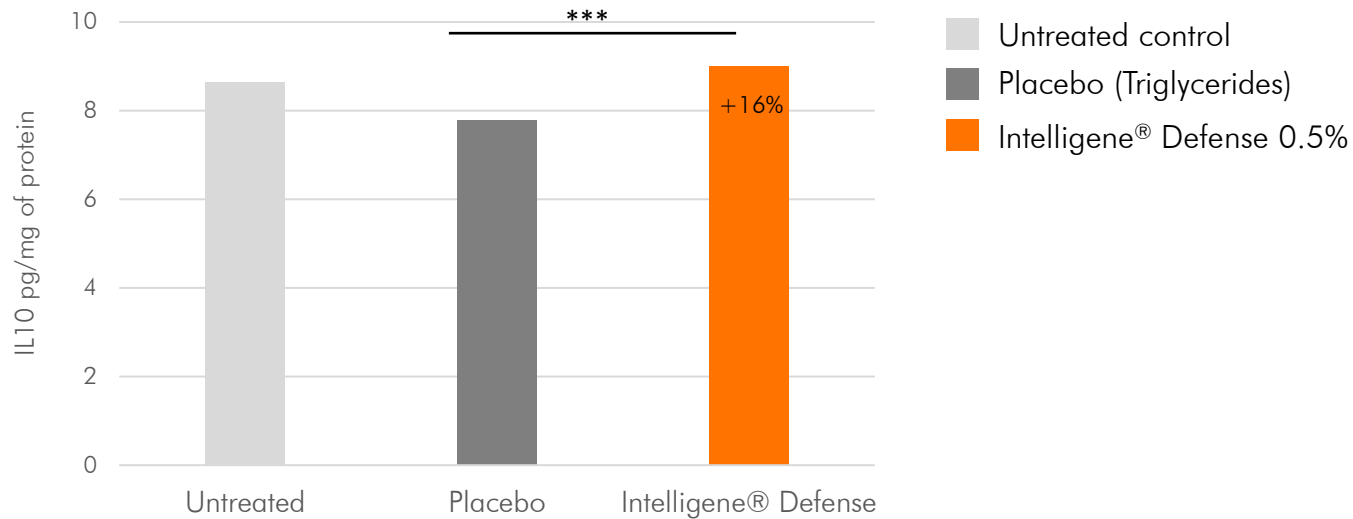


*PMA-Induced Skin Explant Inflammation Model / transcriptomic, Affymetrix analysis
Topical application of INTELLIGENE® DEFENSE 2% versus Placebo, 72 hours.*



REGULATES INFLAMMATORY RESPONSE

INTELLIGENE® DEFENSE activates the expression of the potent anti-inflammatory cytokine Interleukin-10 (IL-10).

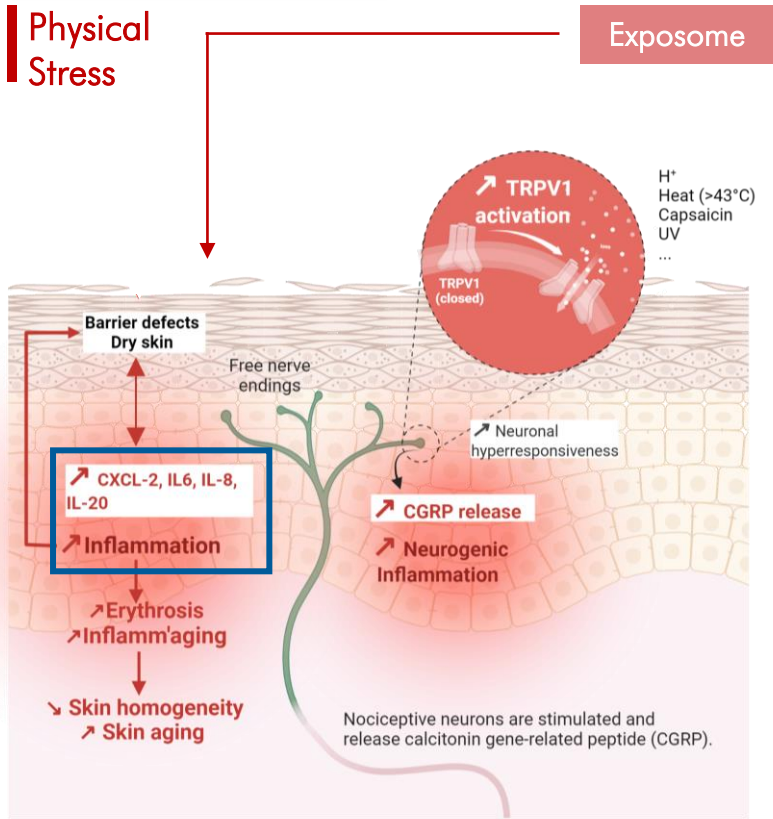


*Skin Explant Model / Protein analysis by ELISA
Topical application of INTELLIGENE® DEFENSE 0.5% versus, 7 days.*

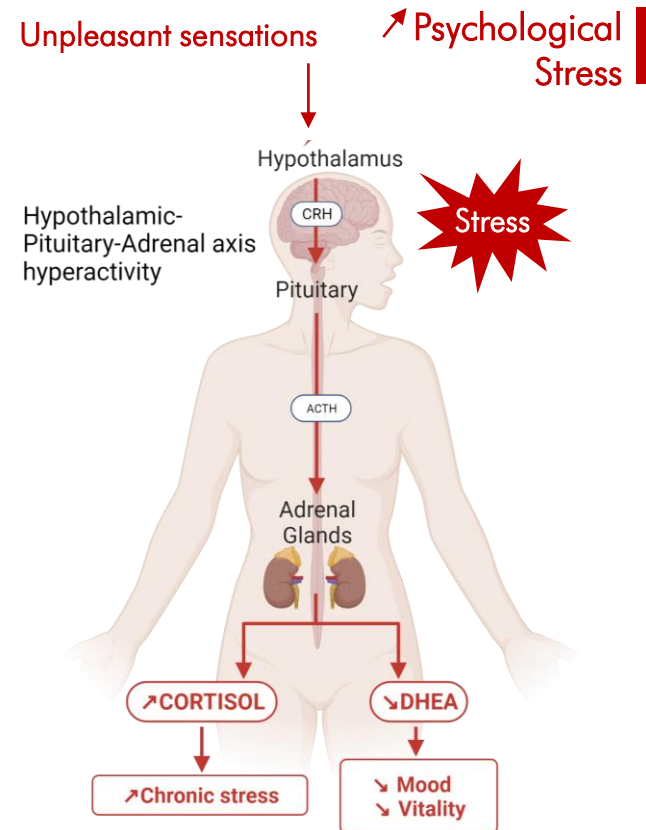
MECHANISM OF ACTION

A systemic approach of sensitive skin

BIOLOGICAL



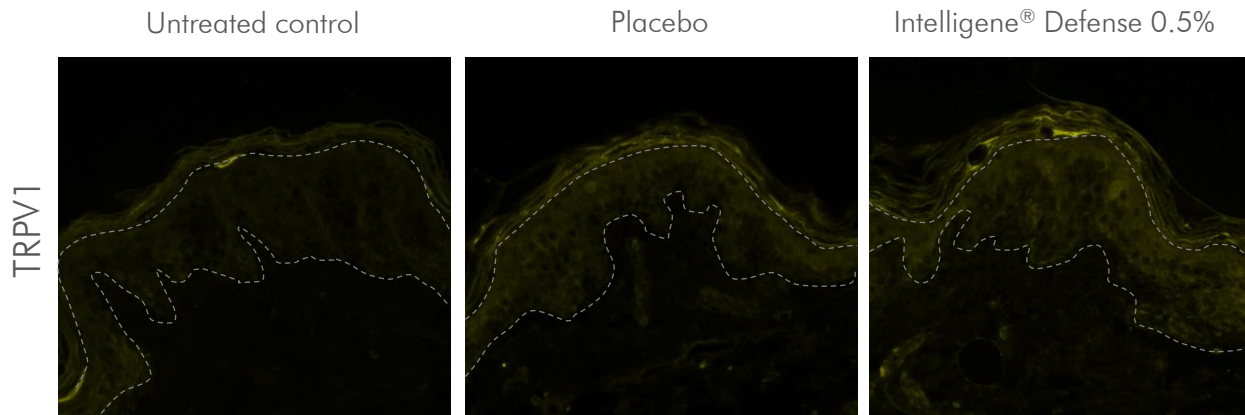
PSYCHONEUROENDOCRINOLOGICAL



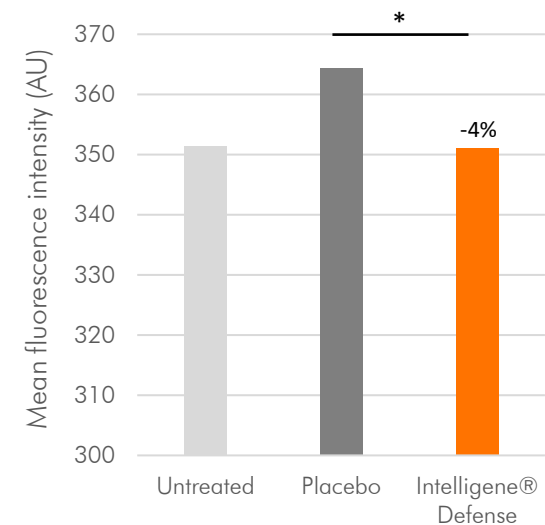


LIMITS NEUROGENIC INFLAMMATION

INTELLIGENE® DEFENSE inhibits the expression of TRPV1, a promising therapeutic target for sensitive skin, skin aging and inflammatory skin diseases.



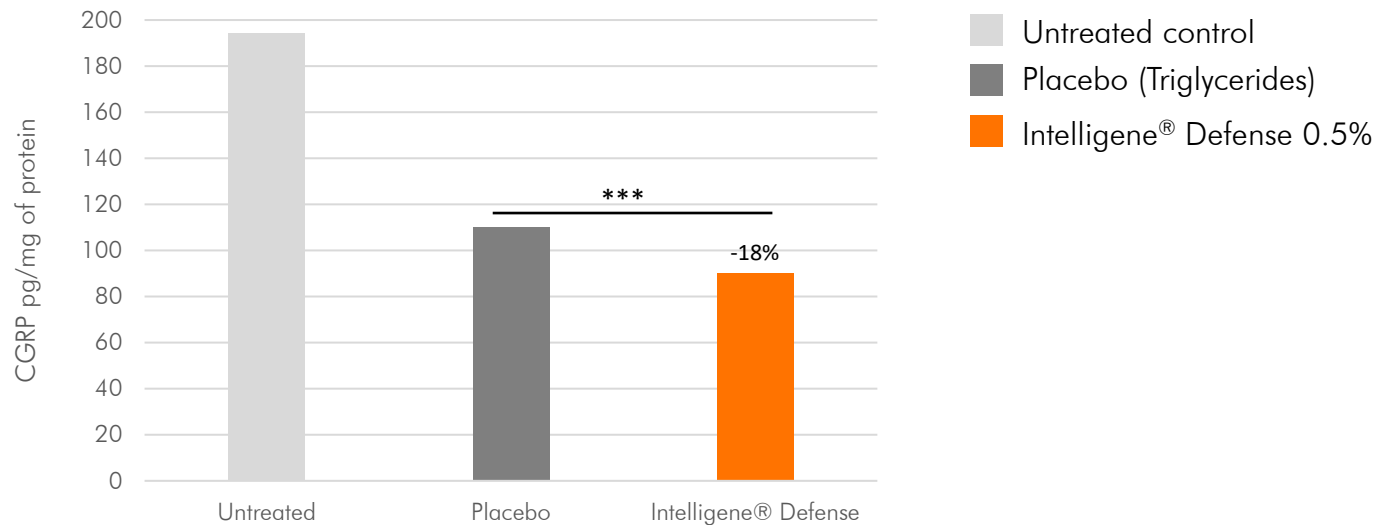
Skin Explant Model / Protein analysis by Immunofluorescence
Topical application of INTELLIGENE® DEFENSE 0.5% versus, 7 days.





LIMITS NEUROGENIC INFLAMMATION

INTELLIGENE® DEFENSE inhibits the release of CGRP, an important contributor of the pathogenesis of neurogenic inflammation, involved in neuronal hyperresponsiveness and hyperreactivity.

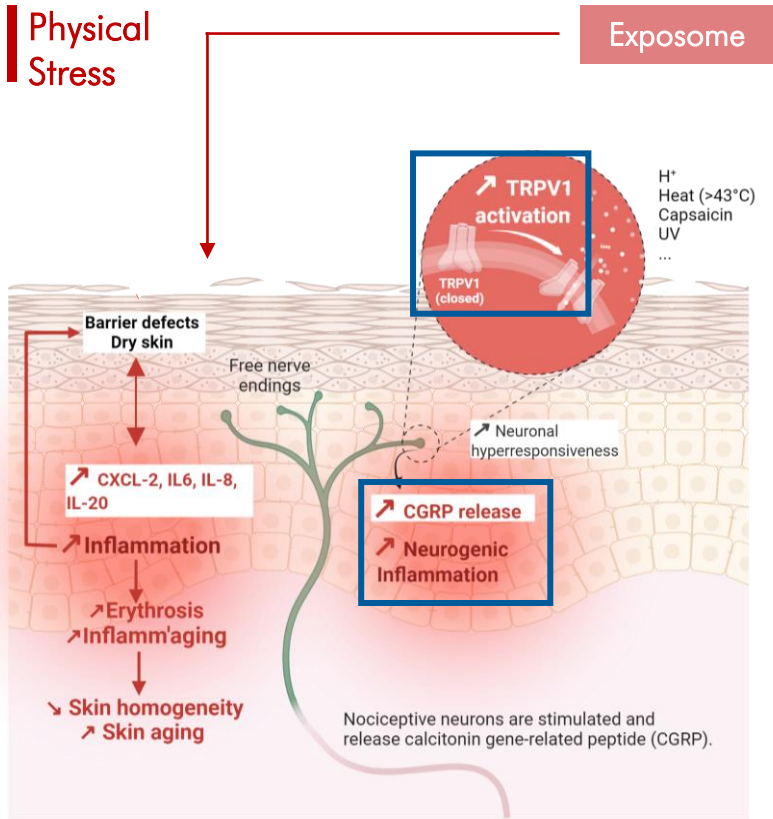


*Skin Explant Model / Protein analysis by ELISA
Topical application of INTELLIGENE® DEFENSE 0.5% versus, 7 days.*

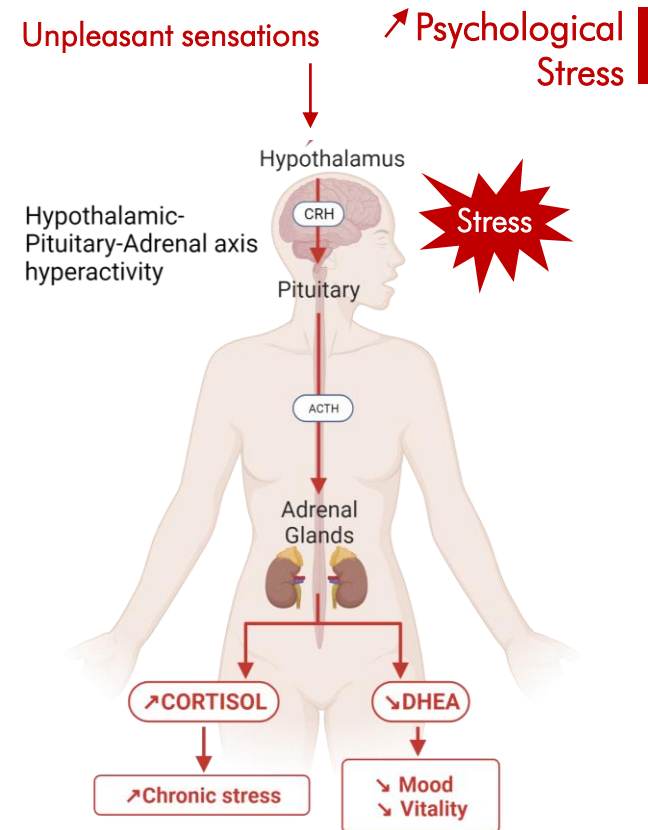
MECHANISM OF ACTION

A systemic approach of sensitive skin

BIOLOGICAL



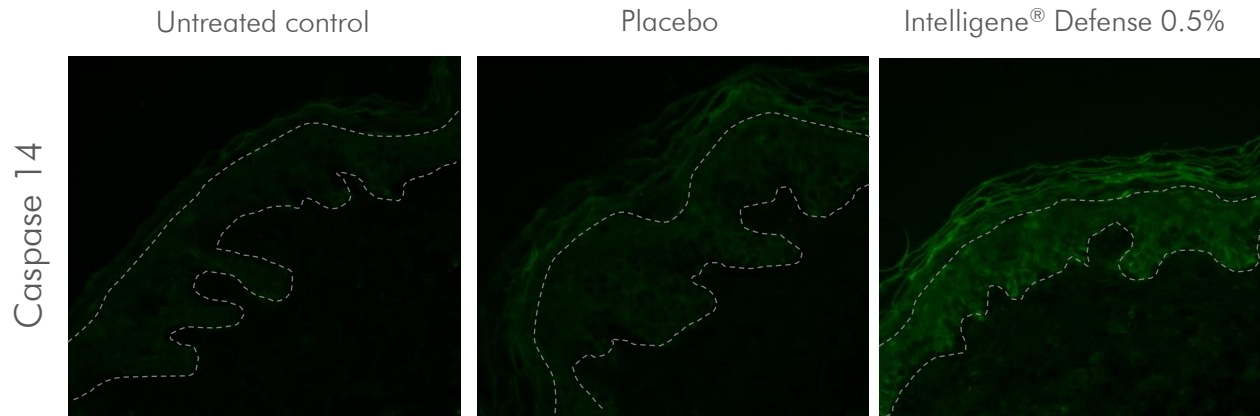
PSYCHONEUROENDOCRINOLOGICAL



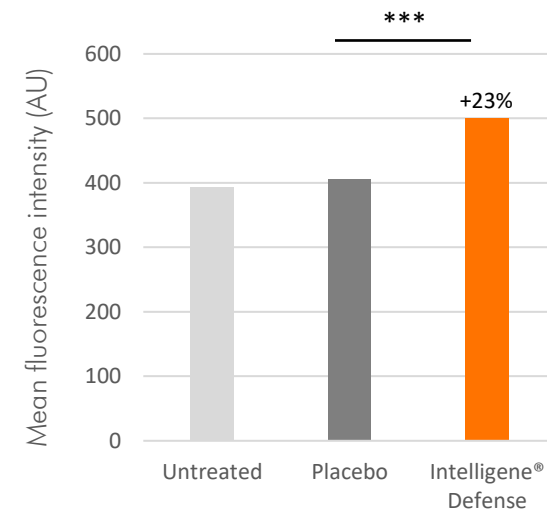


REINFORCES SKIN BARRIER AND HYDRATION

INTELLIGENE® DEFENSE stimulates the expression of Caspase 14, involved in the formation and maintenance of skin barrier, through maturation and proteolysis of filaggrin in Natural Moisturizing Factor (NMF).



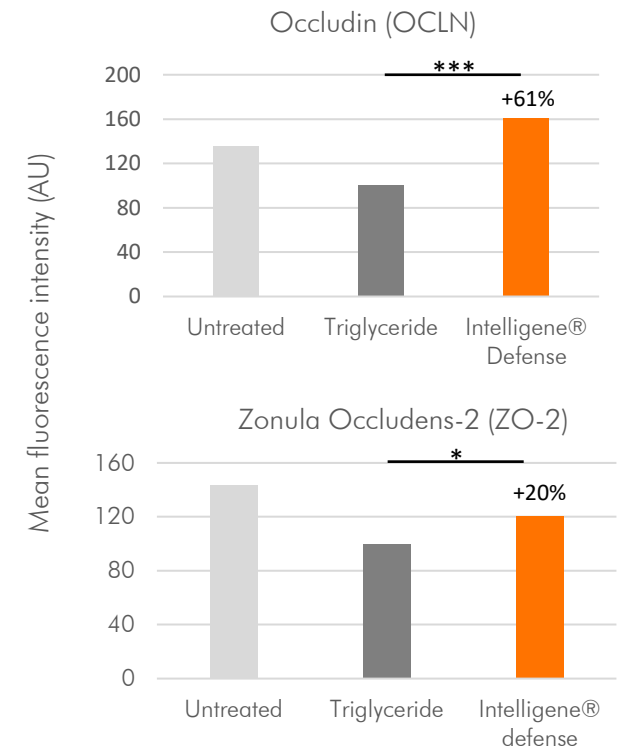
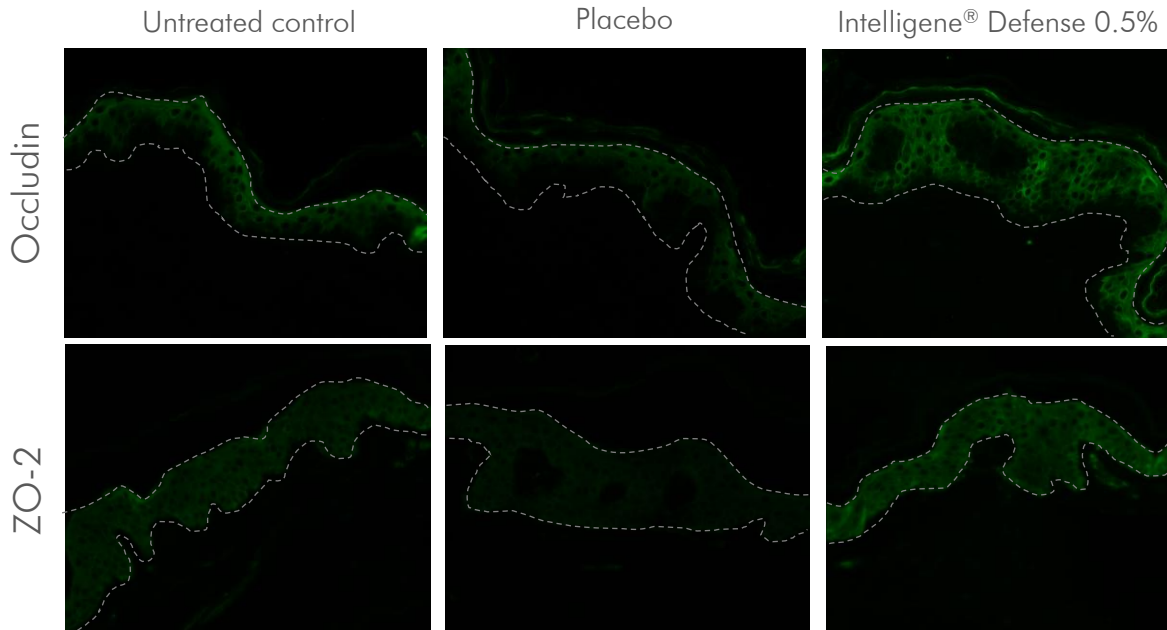
*Skin Explant Model / Protein analysis by Immunofluorescence
Topical application of INTELLIGENE® DEFENSE 0.5% versus, 7 days.*





REINFORCES SKIN BARRIER AND HYDRATION

INTELLIGENE® DEFENSE stimulates the expression of Occludin and Zonula Occludens-2, tight junction components essential for maintenance of epidermal barrier, in the outermost viable layers.

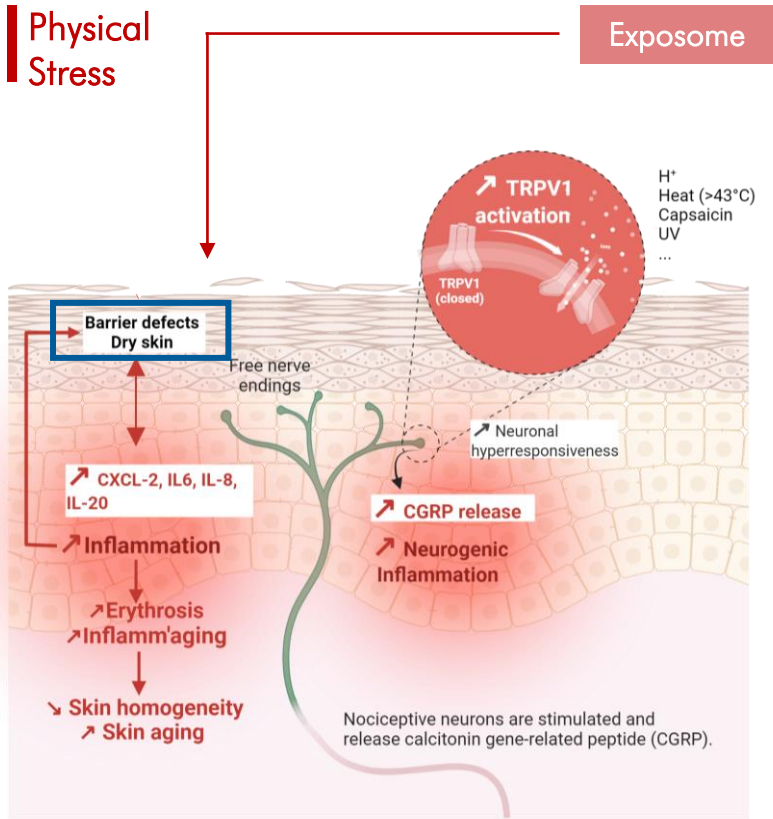


*Skin Explant Model / Protein analysis by Immunofluorescence
Topical application of INTELLIGENE® DEFENSE 0.5% versus, 7 days.*

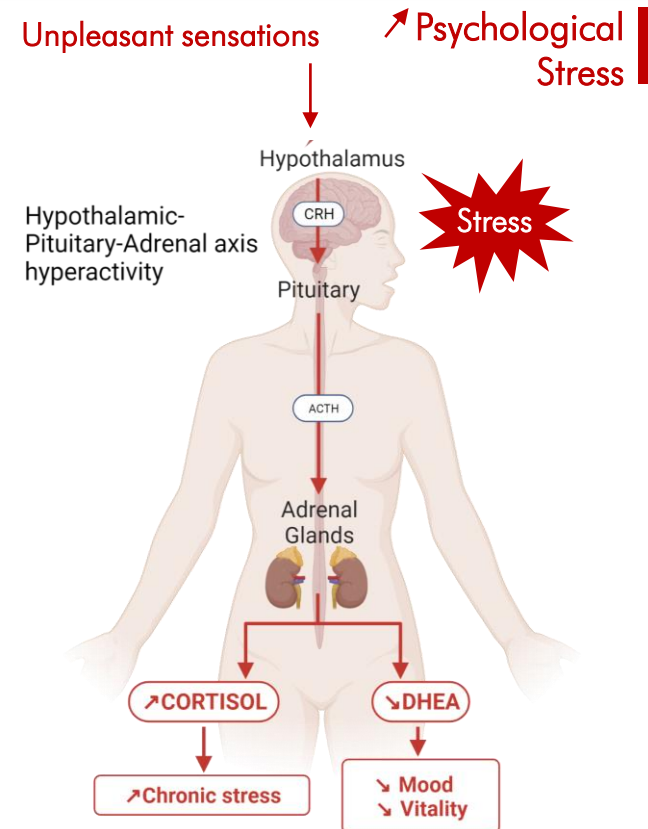
MECHANISM OF ACTION

A systemic approach of sensitive skin

BIOLOGICAL



PSYCHONEUROENDOCRINOLOGICAL



RESUME OF BIOLOGICAL ACTIVITIES

REGULATES INFLAMMATORY RESPONSE

- ↘ Pro-inflammatory mediators (IL6, IL8, IL20, CXCL2, CCL20)
- ↗ Anti-inflammatory cytokine IL-10

LIMITS NEUROGENIC INFLAMMATION

- ↘ TRPV1 expression
- ↘ CGRP release

REINFORCES SKIN BARRIER AND HYDRATION

- ↗ Key factor of Natural Moisturizing Factor production (Caspase 14)
- ↗ Tight junction markers (Occludin, ZO-2)

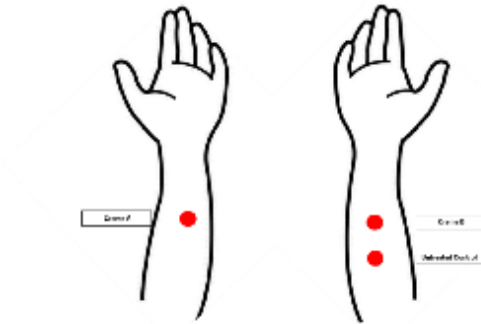


CLINICAL EFFICACY



SOOTHING

- Area of application: **Forearms** with dry and sensitive skin condition
- Stress: Erythema induced by Capsaicin patch – 1h
- Product vs Placebo
- Measurements: **Erythema level, Satisfaction**
- Devices : Mexameter[®], self assessment



1 %
Use

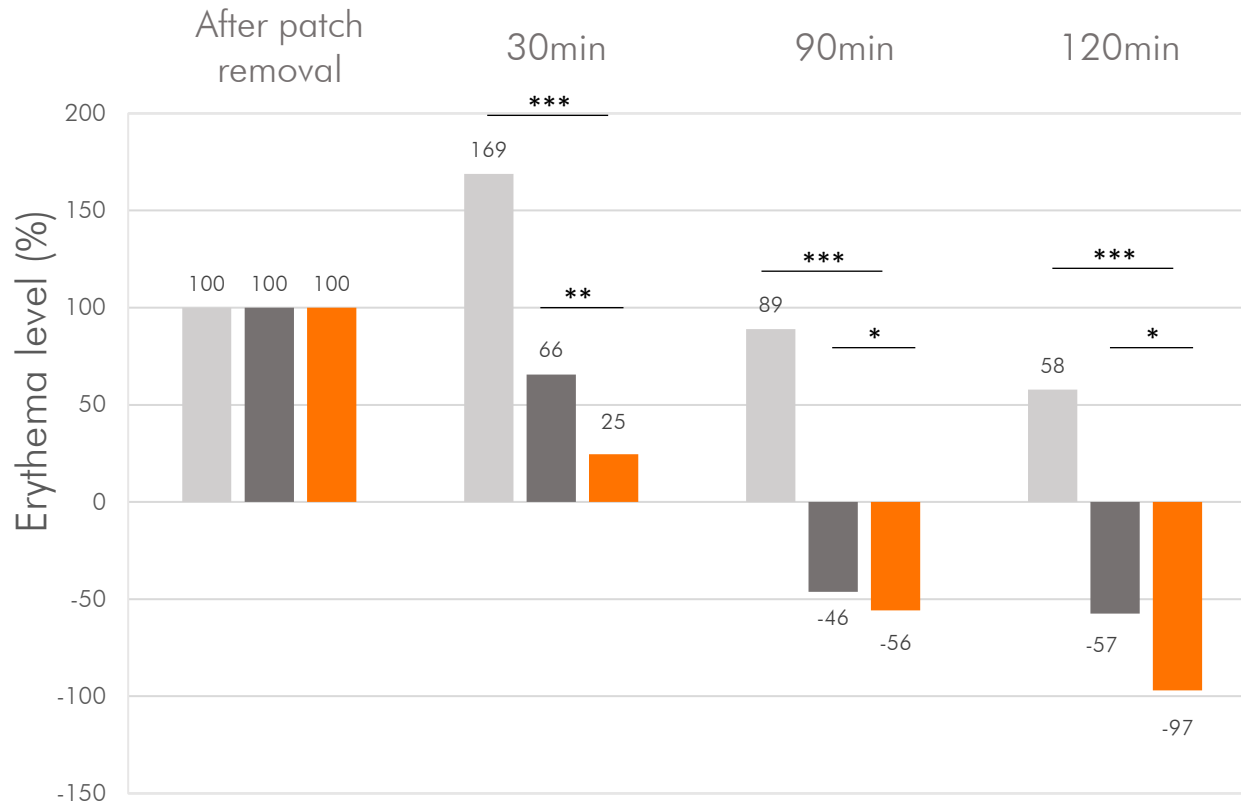
2 
Hours

40  
Volunteers

45-65 Years-old



SOOTHING



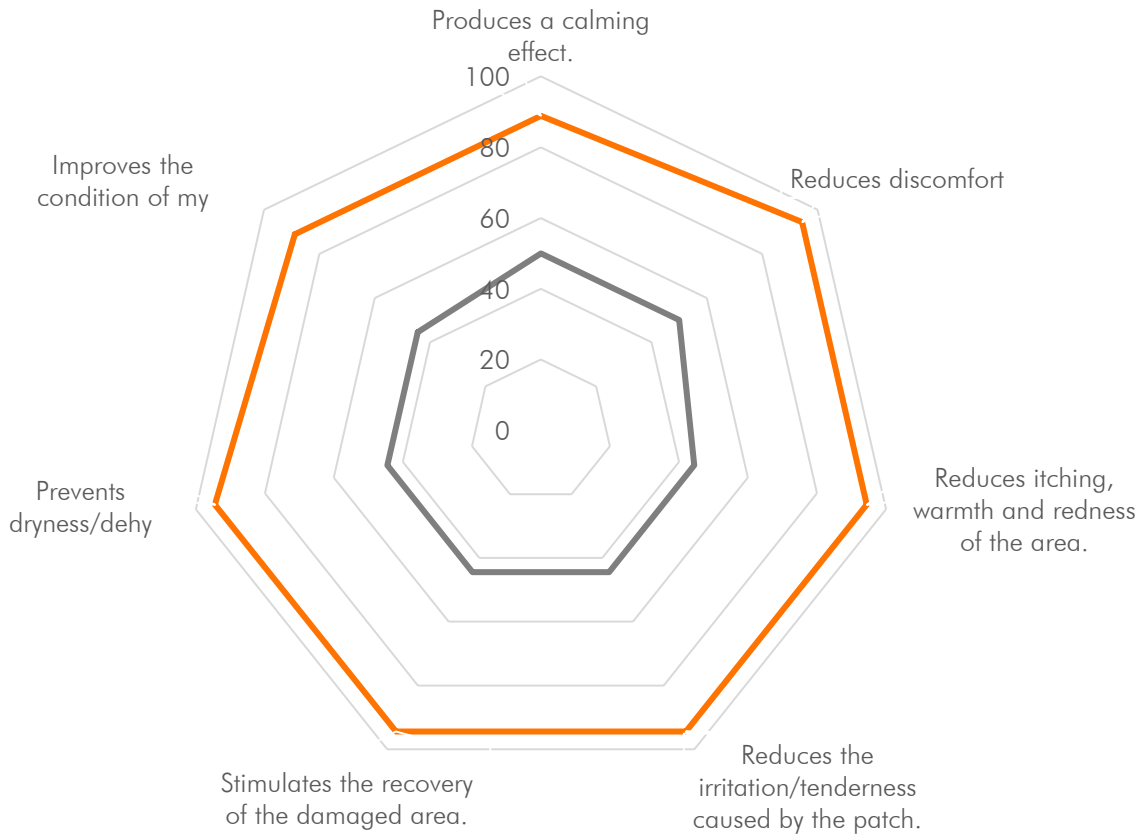
- Untreated control
- Placebo
- Intelligene® Defense 1%

INTELLIGENE® DEFENSE showed a significant decrease of the erythema level at each checkpoint (30, 90 and 120 min) compared to placebo and untreated area analyzed by Mexameter®.

Faster healing of irritated skin



SOOTHING



— Placebo
— Intelligene® Defense 1%

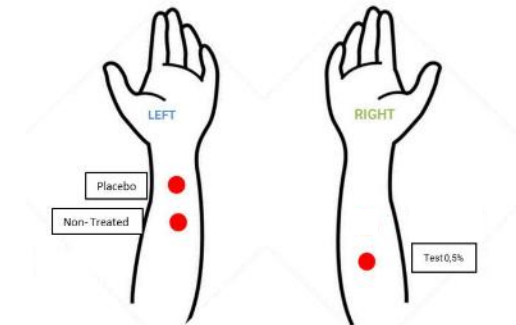
INTELLIGENE® DEFENSE showed a higher level of satisfaction than the placebo, on the various criteria analyzed by self assessment.

Satisfaction improvement



MOISTURIZING – BARRIER

- Area of application: **Forearms** with dry and sensitive skin condition
- Stress: Irritation induces by erosion – 20 rubbing passes
- Product vs Placebo
- Measurements: **Hydration, TEWL, Satisfaction**
- Devices: Corneometer[®], Tewameter[®], Self assessment



0.5 %
Use

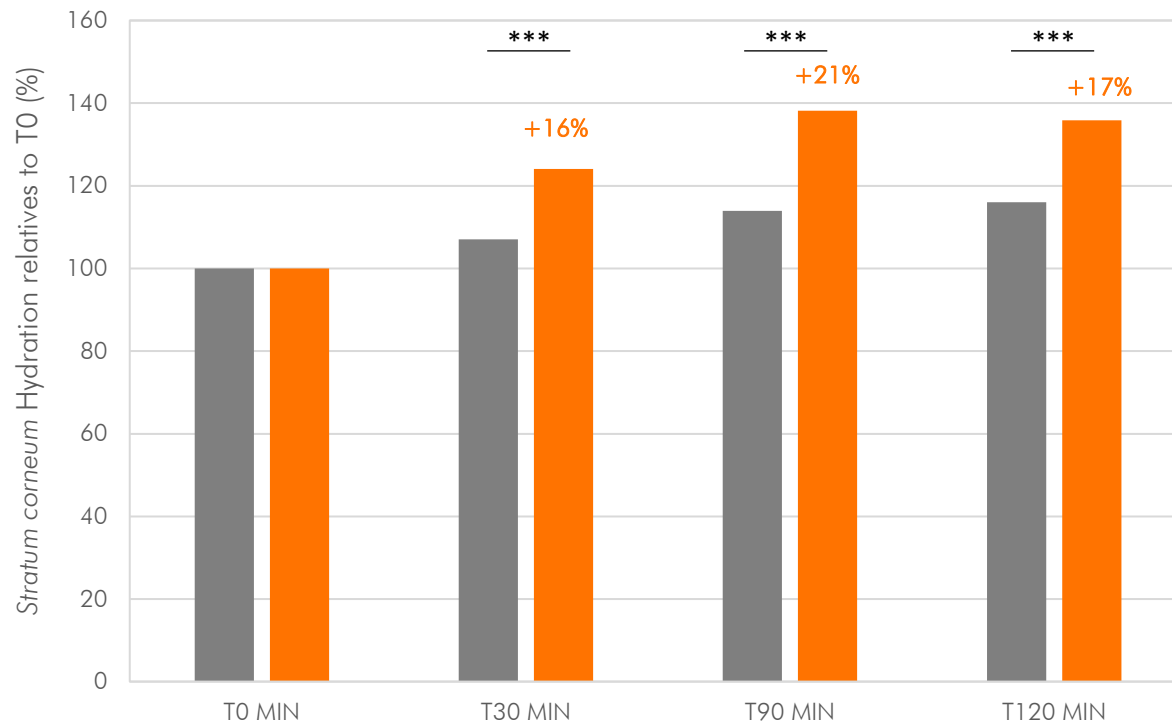
1 
Days

30  
Volunteers

40-70 Years-old



MOISTURIZING – BARRIER



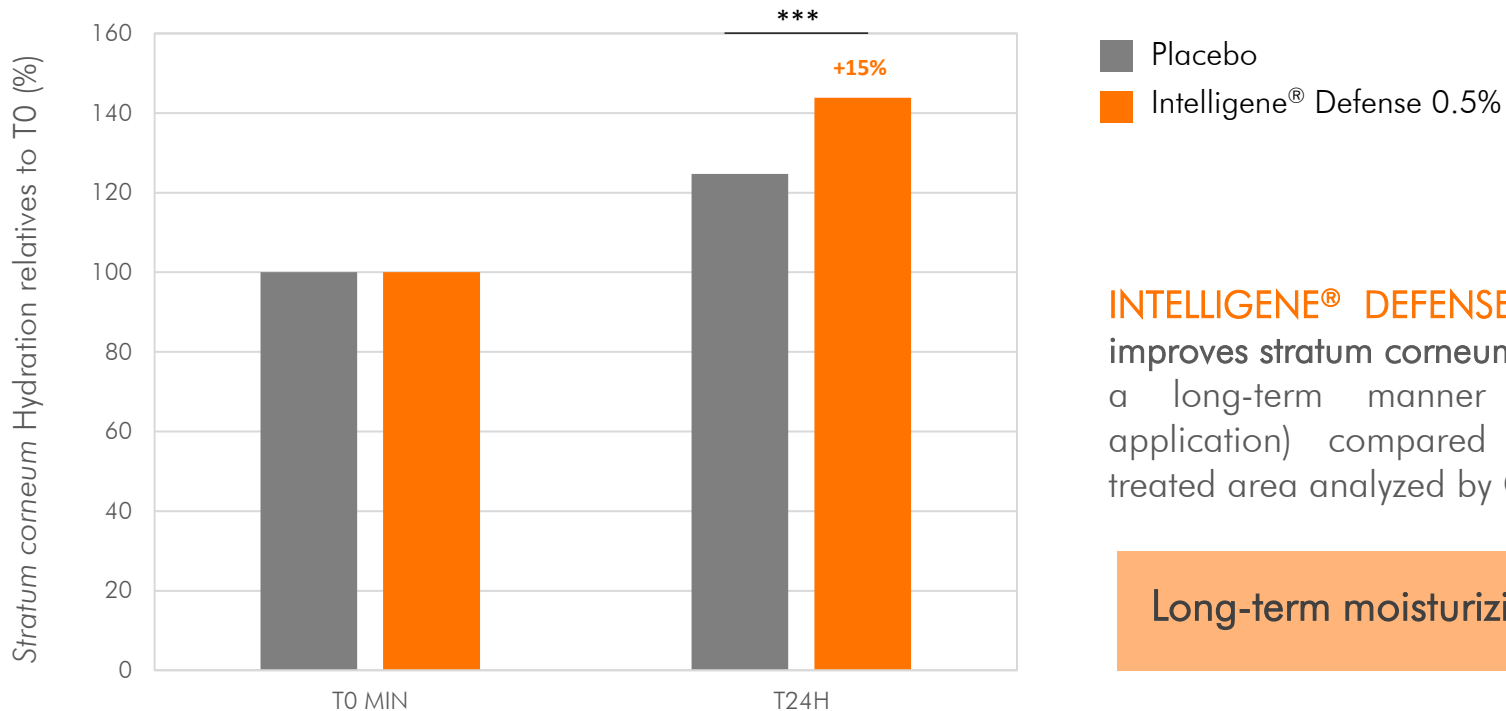
- Placebo
- Intelligene® Defense 0.5%

INTELLIGENE® DEFENSE significantly improves stratum corneum hydration in a short-term manner, at each checkpoint (30, 90 and 120 min) compared to placebo treated area analyzed by Cutometer®.

Short-term moisturizing effect



MOISTURIZING – BARRIER

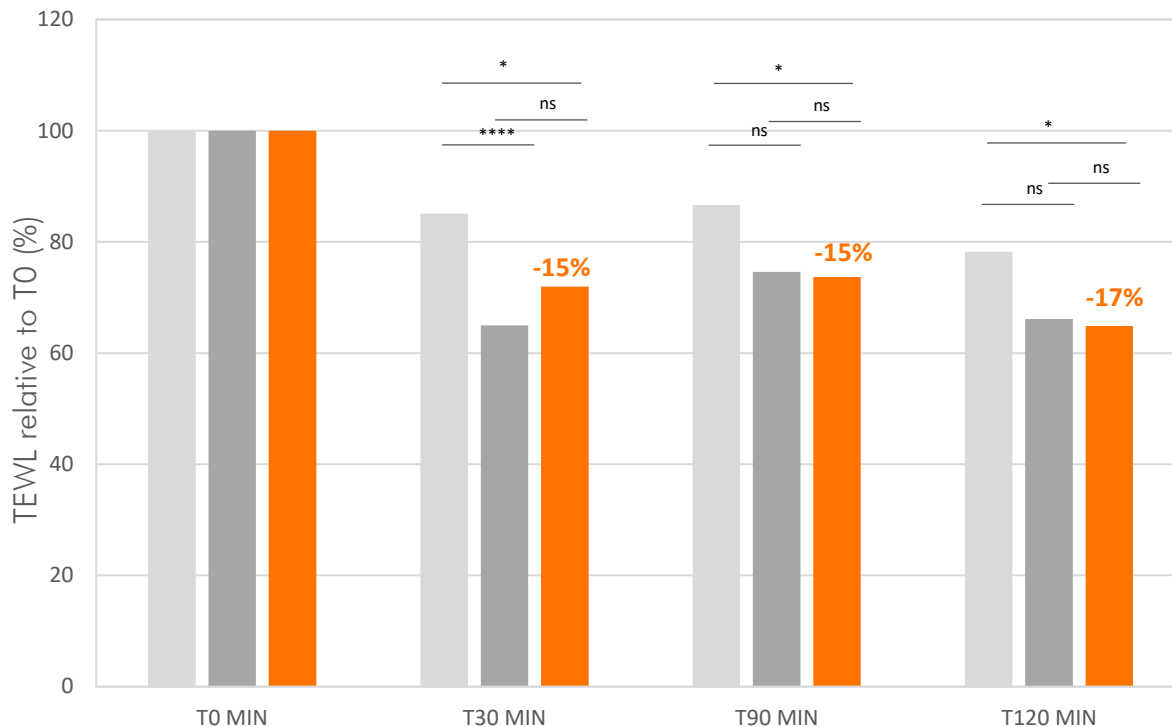


INTELLIGENE® DEFENSE significantly improves stratum corneum hydration in a long-term manner (24h after application) compared to placebo treated area analyzed by Cutometer®.

Long-term moisturizing effect



MOISTURIZING – BARRIER



- Untreated control
- Placebo
- Intelligene® Defense 0.5%

INTELLIGENE® DEFENSE significantly reduces **TransEpidermal Water Loss (TEWL)**, demonstrating, compared to untreated area analyzed by Tewameter®..

Restoration of skin barrier



MOISTURIZING – BARRIER

- Placebo
- Intelligene® Defense 0.5%

INTELLIGENE® DEFENSE showed a higher level of satisfaction than the placebo, on the various criteria analyzed by self assessment.

Satisfaction improvement





ANTI-REDNESS, ANTI-AGING

- Area of application: **Face** with sensitive and stinging skin condition
- Product vs Placebo
Group Placebo n=10 - Group Product n=25
- Measurements:
 - Erythrosis by scoring (2D and 3D)
 - Depth of a crow's feet wrinkle (LifeViz Micro)
 - Skin homogeneity by scoring
 - Acceptability self-questionnaire D28
 - Tolerance by dermatological evaluation



0.5 %
Use

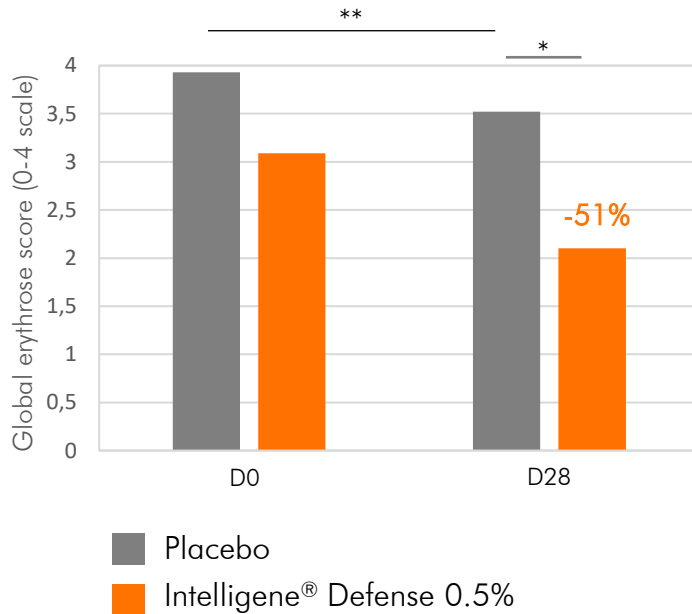
28 
Days

35  
Volunteers

40-65 Years-old



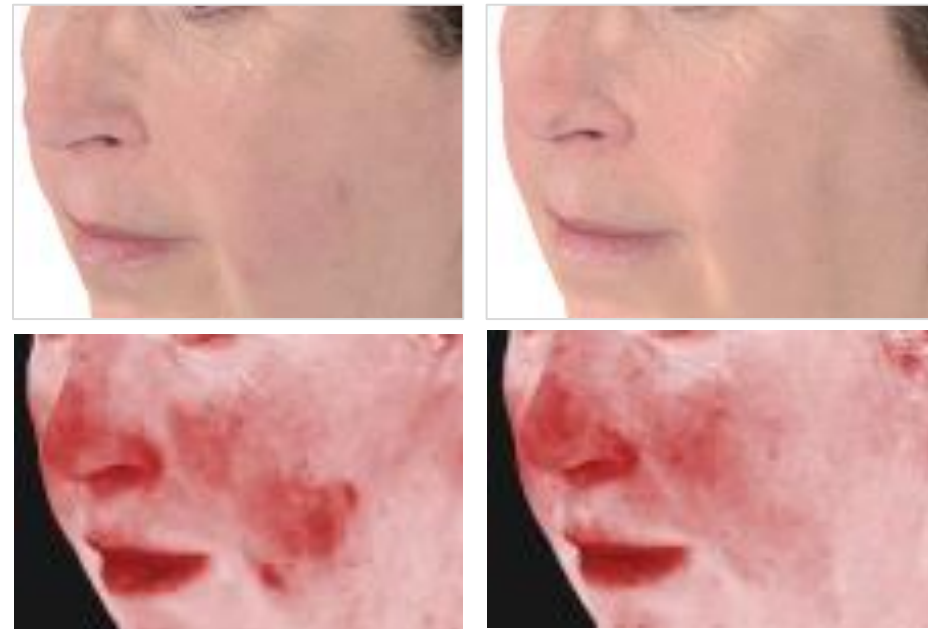
ANTI-REDNESS, ANTI-AGING



INTELLIGENE® DEFENSE significantly decreases the erythrosis compared to D0, demonstrating a soothing effect on sensitive skin.

D0 -Volunteer 27

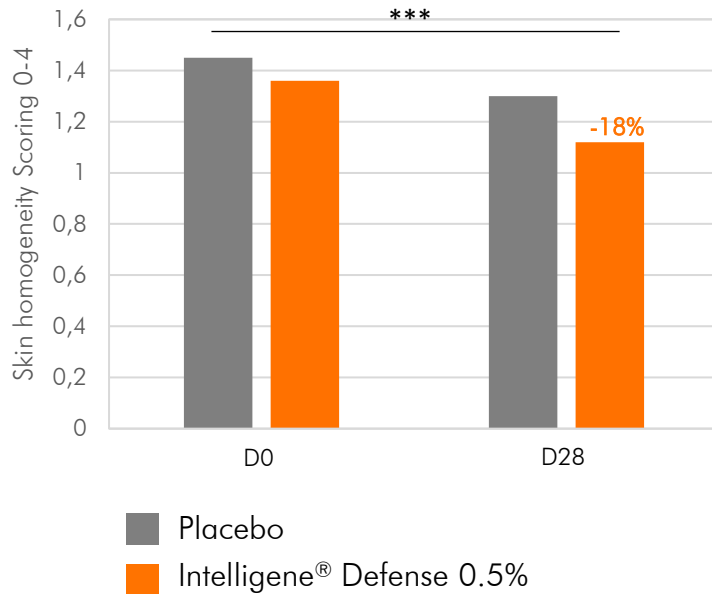
D28 -Volunteer 27



Anti-redness effect



ANTI-REDNESS, ANTI-AGING



D0 -Volunteer 14



D28 -Volunteer 14

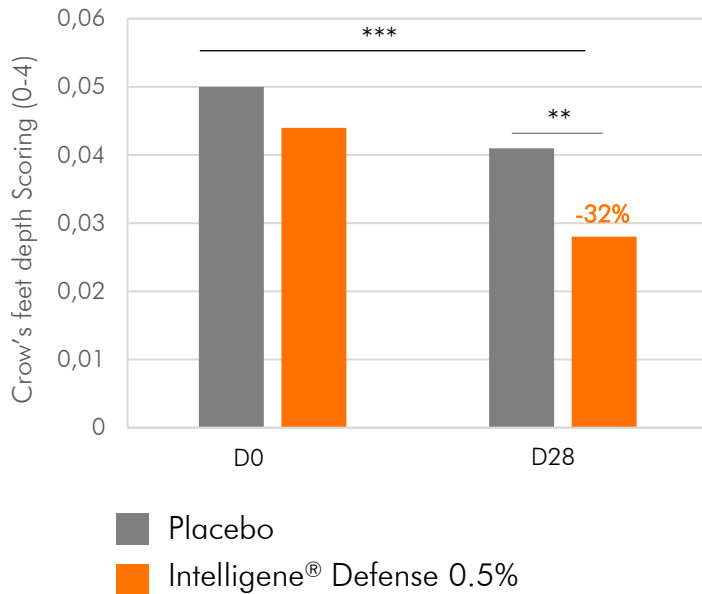


Skin homogeneity improvement

INTELLIGENE® DEFENSE significantly decreases the clinical homogeneity score compared to D0, demonstrating an improvement in skin homogeneity.



ANTI-REDNESS, ANTI-AGING



D0 -Volunteer 35



D28 -Volunteer 35



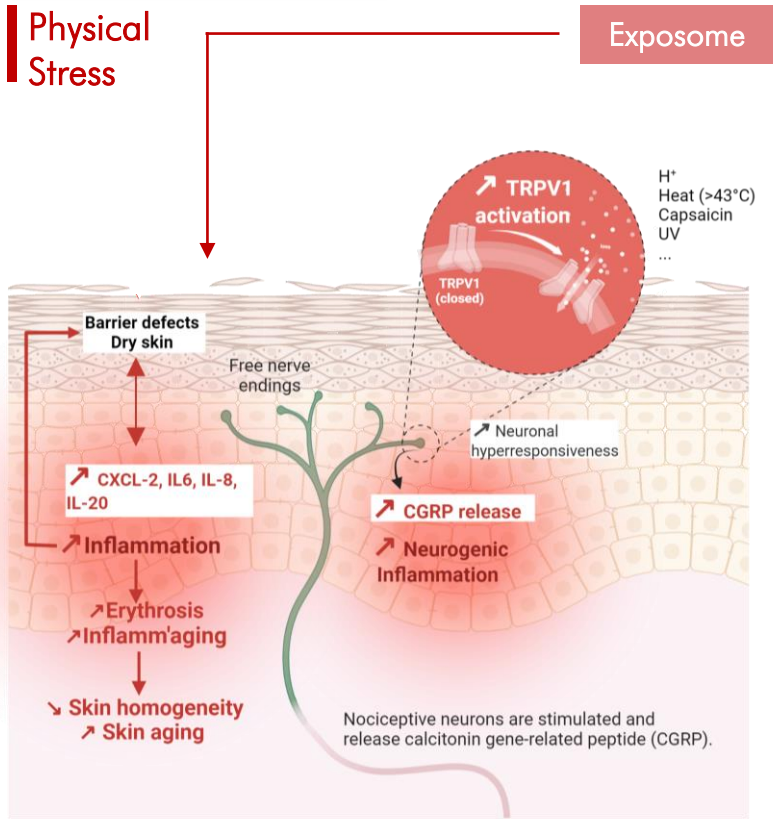
Anti-wrinkles effect

INTELLIGENE® DEFENSE significantly decreases the crow's feet depth compared to D0 and placebo, demonstrating an anti-aging effect.

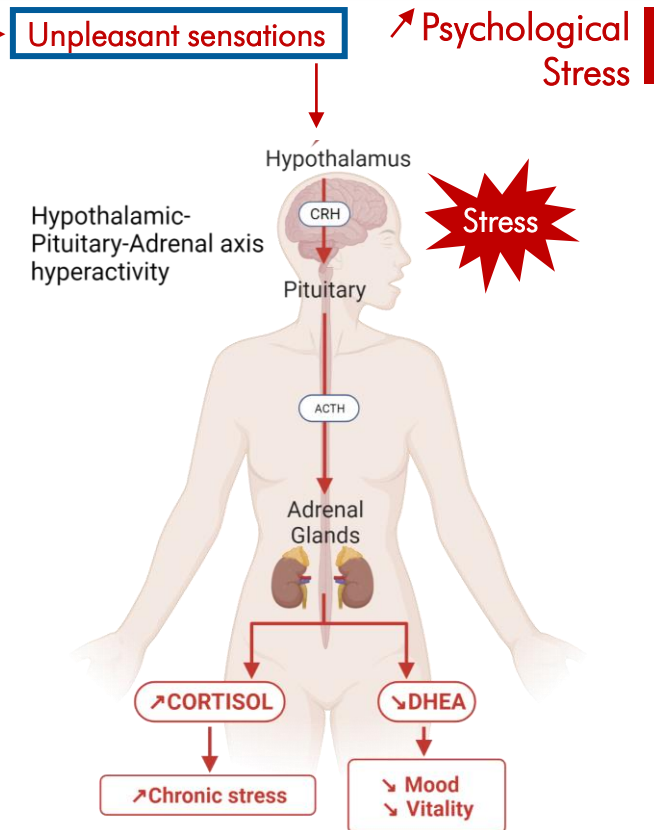
MECHANISM OF ACTION

A systemic approach of sensitive skin

BIOLOGICAL



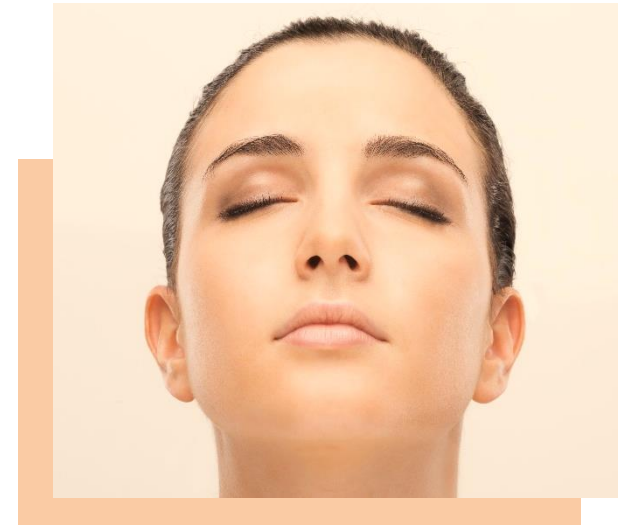
PSYCHONEUROENDOCRINOLOGICAL





PSYCHOBIOLOGICAL WELL-BEING

- Area of application: **Face** with sensitive and stinging skin condition
- Product vs Placebo
Group Placebo n=10 – Group Product n=25
- Measurements:
 - Salivary **Cortisol** and **DHEA**
 - **Self-Manikin Assessment (SMA)** protocol
A nonverbal tool to express enjoyment/pleasure.
 - **Brief Mood Introspection Scale (BMIS)** protocol
Protocol based on Verbal answers: a set of sixteen emotional adjectives with four values ranging to assess pleasant emotions.



0.5 %
Use

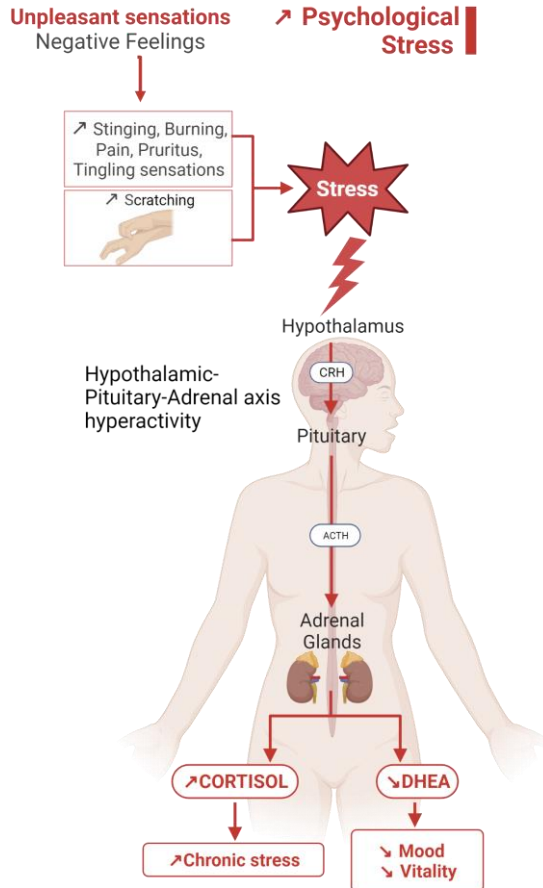
28 
Days

35  
Volunteers

40-65 Years-old



PSYCHOBIOLOGICAL WELL-BEING



Cortisol and DHEA are Physiological mediators of the Hypothalamo-Pituitary axis (HPA)

Measurable in saliva upon awakening and correlated with plasma levels:

- Cortisol Awakening Response (CAR)
- DHEA Awakening Response (DAR)

Measurement of the total hormone concentration versus time-dependent change:

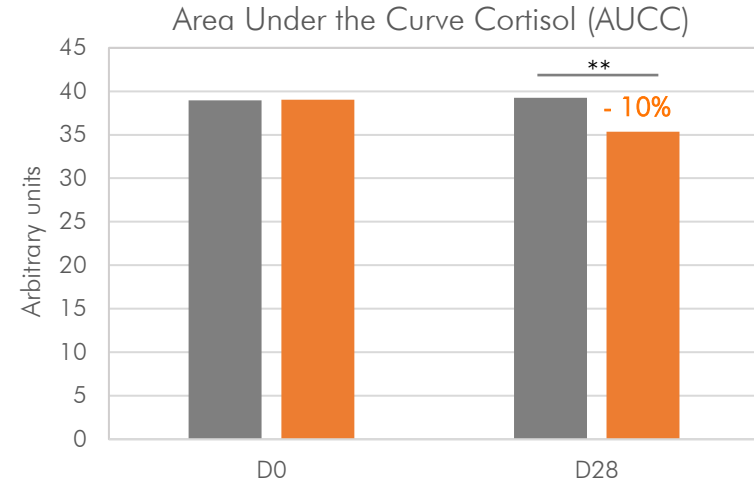
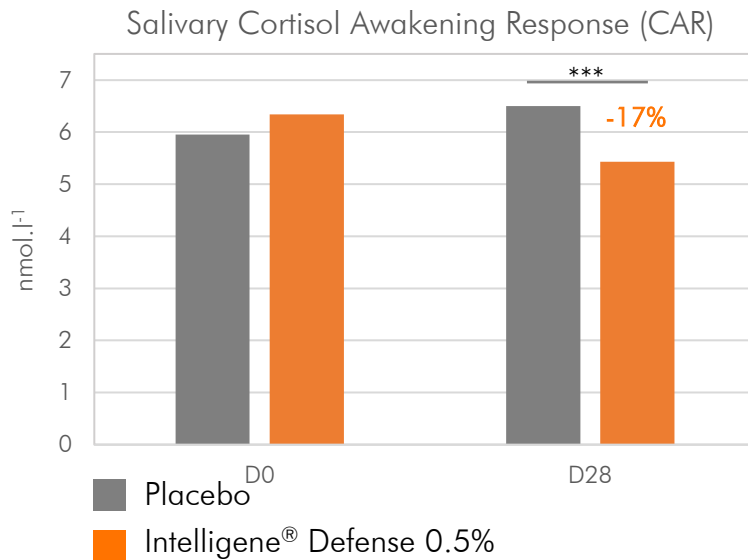
- Areas Under the Curve for Cortisol (AUCC) and DHEA (AUCDHEA).

(Lac et al. 1993)
(Pruessner et al. 2002)



PSYCHOBIOLOGICAL WELL-BEING

INTELLIGENE® DEFENSE significantly decreases the CAR and the AUCC, reflecting positive psychological traits.

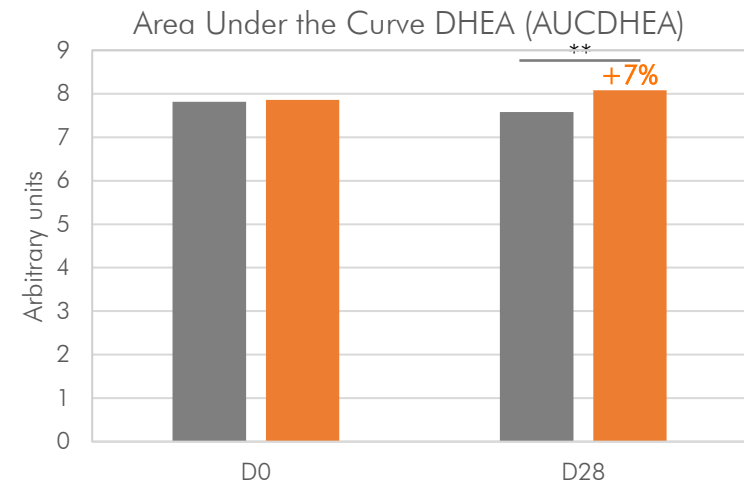
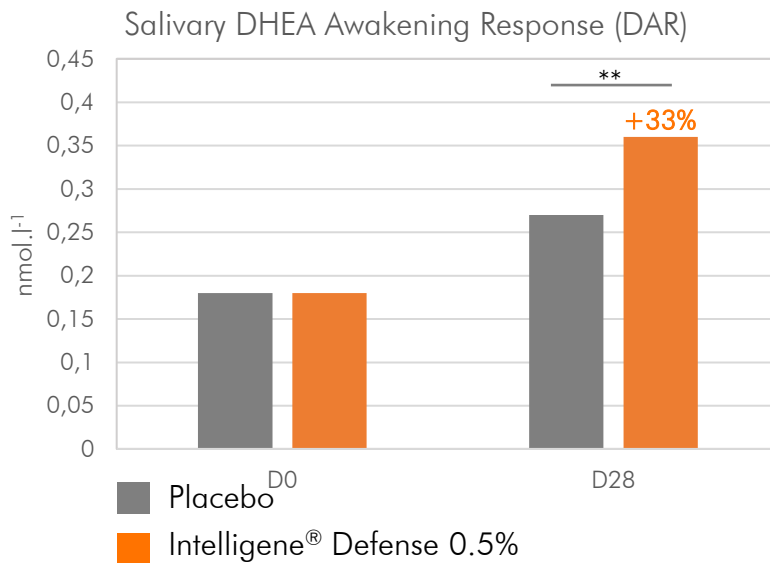


Positive psychological features



PSYCHOBIOLOGICAL WELL-BEING

INTELLIGENE® DEFENSE significantly decreases the in the DAR and the AUCDHEA reflecting elevate mood, calm emotions, increased alertness and vitality.

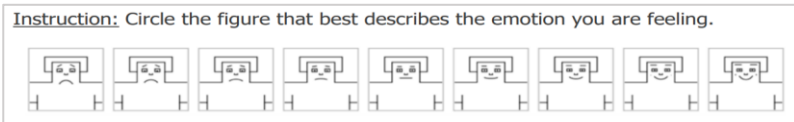


Positive psychological features



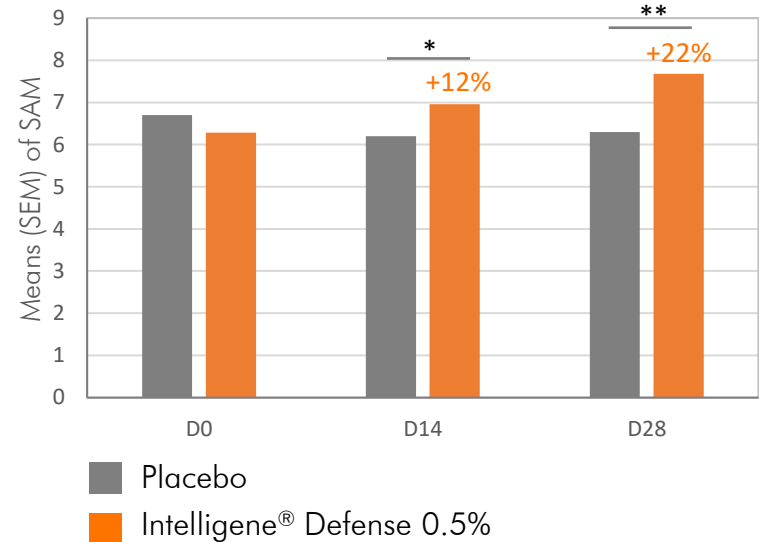
PSYCHOBIOLOGICAL WELL-BEING

Self-Assessment Manikin (SAM): an emotion assessment with a nonverbal tool



(Bradley MM, Lang PJ, 1994)

INTELLIGENE® DEFENSE induces significant differences for pleasure/enjoyment emotion at day 14 and 28 compared to the placebo cream.

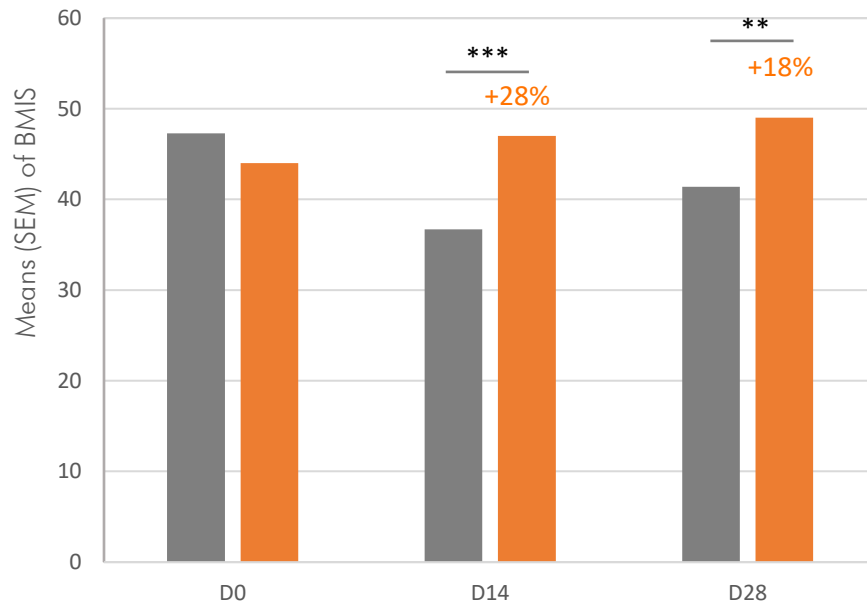


Improvement in emotions felt



PSYCHOBIOLOGICAL WELL-BEING

Brief Mood Introspection Scale (BMIS): an emotion assessment with a verbal tool.
→ four values ranging from "not at all" to "completely" to assess pleasant emotions:



■ Placebo
■ Intelligene® Defense 0.5%

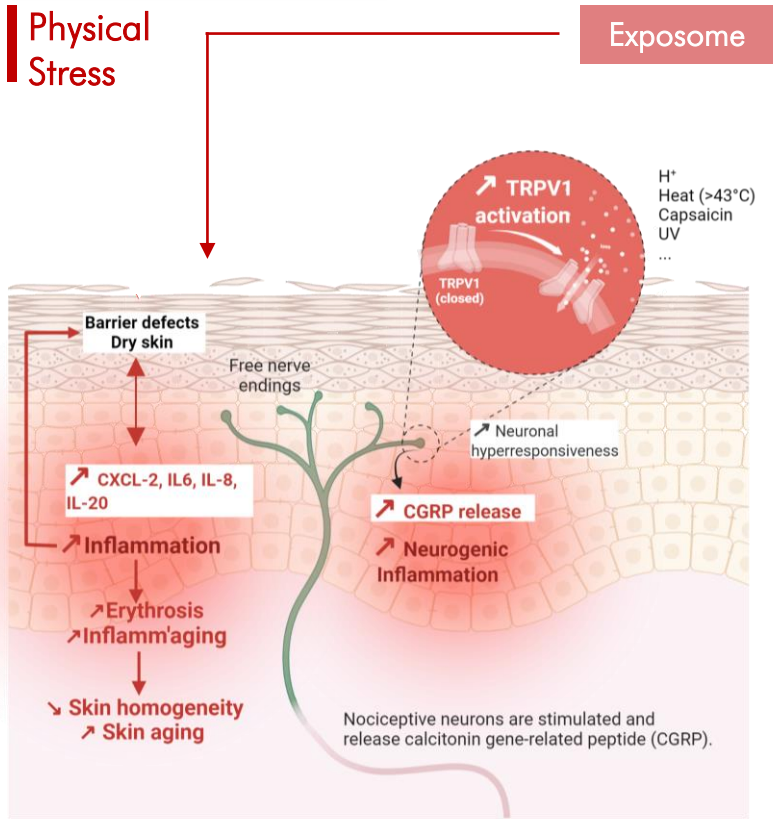
INTELLIGENE® DEFENSE induces a significant evolution of positive emotions at day 14 and 28 compared to the placebo cream.

Improvement in emotions expressed

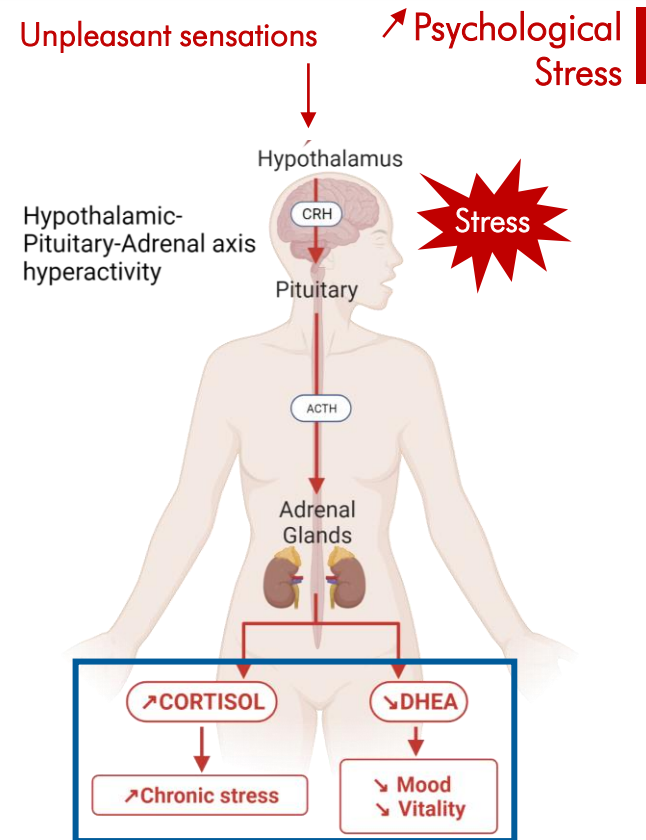
MECHANISM OF ACTION

A systemic approach of sensitive skin

BIOLOGICAL



PSYCHONEUROENDOCRINOLOGICAL



RESUME OF CLINICAL EFFECTS

SOOTHING EFFECT / ANTI-(NEUROGENIC) INFLAMMATION

- ↘ Capsaicin-induced erythema and irritation
- ↘ Itching
- ↘ Erythrosis
- ↗ Skin homogeneity
- ↘ Skin aging

RESUME OF CLINICAL EFFECTS

MOISTURIZING EFFECT AND SKIN BARRIER RESTORATION

- ↗ Hydration in Stratum Corneum of damaged dry skin
- ↗ Appearance of skin improved
- ↘ TEWL in damaged skin barrier by erosion

WELLBEING ENHANCING: ATTENUATION OF STRESS LEVEL / REGULATION OF HPA AXIS

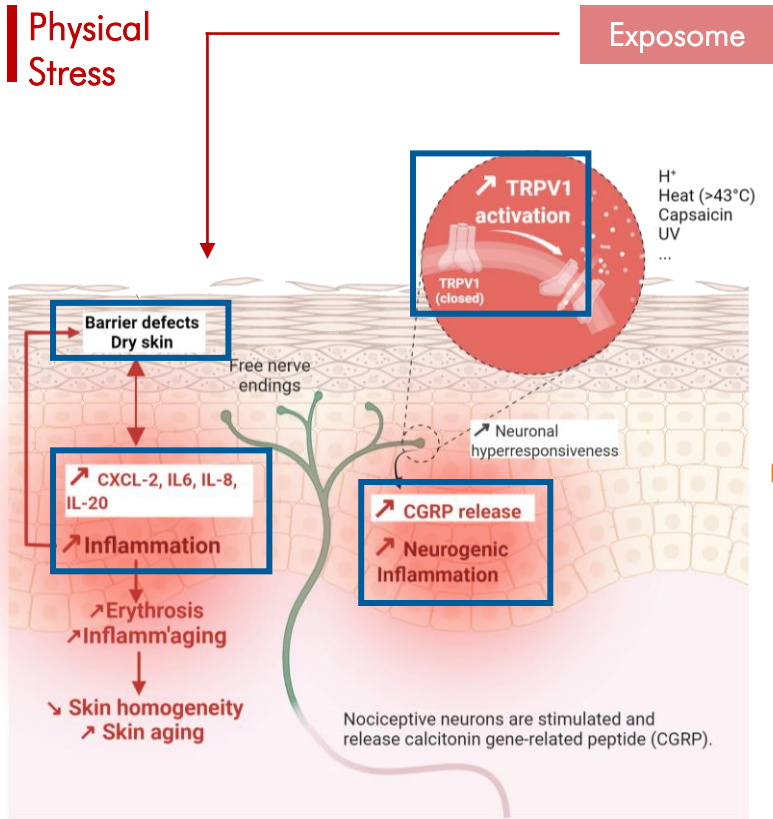
- ↘ Stress (↘ Cortisol)
- ↗ Calm emotions, positive mood, vitality (↗ DHEA, ↗ SAM, ↗ BMIS)

MECHANISM OF ACTION

A systemic approach of sensitive skin

BIOLOGICAL

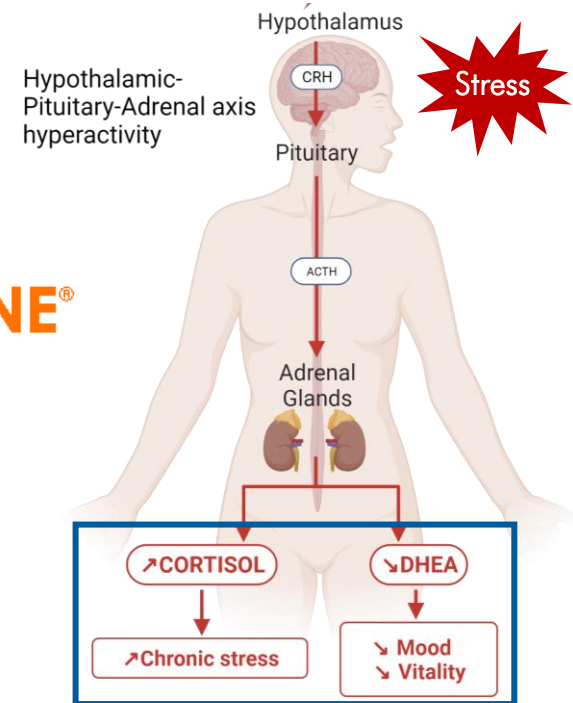
Physical Stress



PSYCHONEUROENDOCRINOLOGICAL

Unpleasant sensations

Psychological Stress



INTELLIGENE[®]
DEFENSE

TECHNICAL INFORMATION

INCI: *Solanum Lycopersicum* (Tomato) Fruit Lipids

APPLICATION

- Face care
- Body care
- Sun care
- Sensitive skin

DOSE OF USE

0.5-2%

ASPECT

Viscous light orange to reddish liquid

SOLUBILITY

Oil Soluble

ODOR

Characteristic odor



INTELLIGENE® Defense is a raw material verified by ECOCERT Greenlife, conform to the COSMOS standard.