ACTIVE BEAUTY

Neuroglow™

The active for glow and good mood

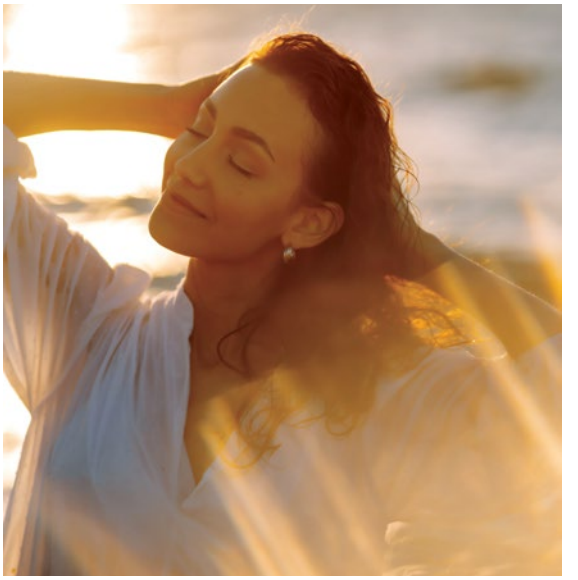
Well in my body / Bio tanning

Givaudan

Human by nature

Focus on the product

The beneficial power of sunshine



Sunlight is a source of health, good mood and energy.

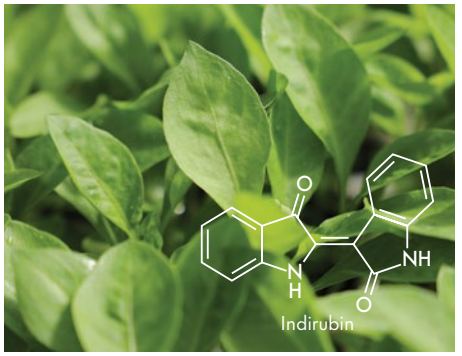
Sunlight is essential for human health and well-being: many people enjoy the feeling of sunlight, and there is increasing evidence that supports its many health benefits.

Sunlight has been recognised to have a positive impact on our mood and energy, besides of course the promotion of Vitamin D production; it is also promoting a healthy aspect thanks to the tan and bronzed look that is seeked for by consumers[1]. As modern life brings us to spend more time indoors, there is a growing quest from consumers for the benefits of being in the sun, for that very special sensation of feeling and looking happy and healthy.

On the other hand, excessive exposure to sunlight can trigger photoageing, inflammation and DNA damage.

Botanicals can mimick the molecular benefits of sun: Neuroglow™

Plants contain bioactive molecules that are still largely unexplored and would trigger health research in this realm. Our scientists in R&D Green Fractionation have been able to identify and optimise a cosmetic active ingredient that is capable of mimicking all the benefits of the sun, preparing our skin for sun exposure and counteracting the potential overexposure side effects.



Neuroglow™ derives from the plant *Persicaria tinctoria* (syn: *Polygonum tinctorium*) from a fully traceable supply chain established in Provence (France).

The supply chain has been optimised for the cultivation in this region and for the best yield of the bioactive molecules thanks to our agronomy expertise.

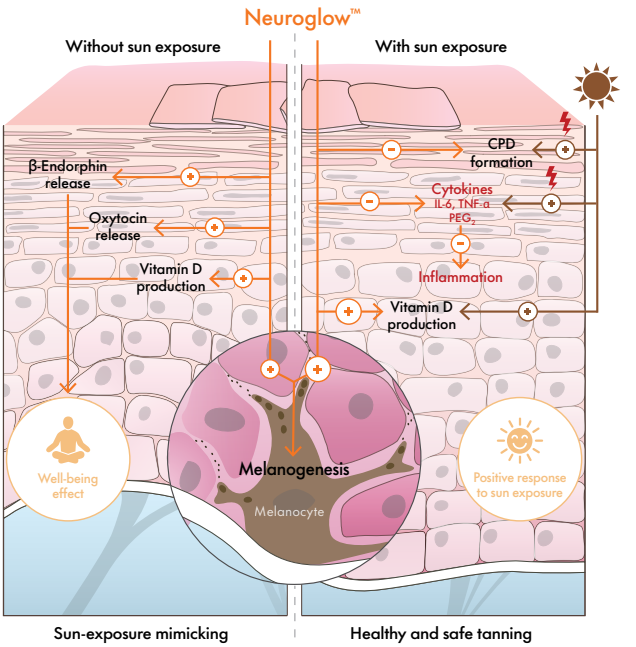
The leaves are processed fresh to transform a precursor molecule called indican in **Indirubin**, our bioactive marker and active molecule, which is selectively extracted and standardised in Neuroglow™, solubilised in an optimised natural carrier (Moringa oil) and stabilised with a natural antioxidant (Rosemary extract).

Neuroglow™: the first molecular sun for beauty

Neuroglow™, by boosting melanin and well-being molecules like Beta-endorphin, Vitamin D and Oxytocin, mimics all the good properties from the sun[2-4]:

- Prepares the skin for a healthy sun exposure.
- Boosts the production of protective melanin, protanning.
- Boosts well-being and energy.
- Prevents sun-driven inflammation damage and promotes DNA protection.

Neuroglow™ is the ideal active ingredient to provide a quick and efficient solution to give the skin a healthy glow, while uplifting mood and positive emotions.



[1] Mead N., 2008 May; [2] Tran et al, 2008; [3] Fell et al, 2014; [4] Nguyen, 2018

Biological activity

Neuroglow™ triggers genes connected to pigmentation, well-being and protection

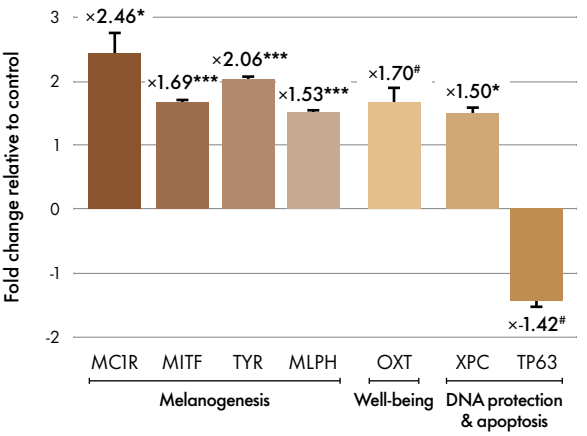
Skin explants were treated with Neuroglow™ at 0.8% in the vehicle (Miglyol) for 5 days; total RNA were extracted and retro-transcripted to cDNA. Targeted genes expression were analysed and quantified by using RT-qPCR. Data are expressed relative to vehicle alone.

Results: Genes linked to melanogenesis (MC1R, MITF, TYR, MLPH) were upregulated by up to 2.5x.

Gene coding for DNA protection biomarkers were upregulated by 1.5x (XPC) and apoptosis was limited by downregulation of TP63 gene.

Oxytocin expression was also upregulated (1.7x).
All the observed data confirm the potential pro-pigmenting, skin protecting and well-being properties of Neuroglow™.

Transcriptomic analysis



Student t test: #p<0.1, *p<0.05, ***p<0.001

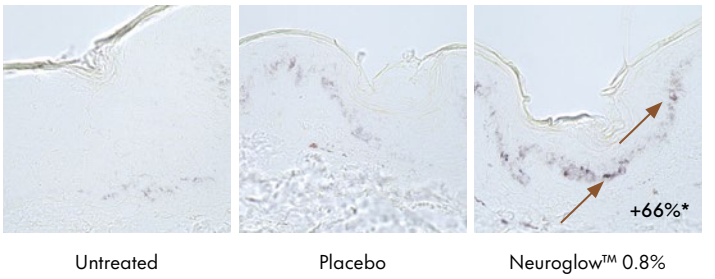
Neuroglow™ safely activates the melanogenesis pathway

1. Neuroglow™ boosts melanogenesis without sun exposure

Skin explants were topically treated for 5 days with Neuroglow™ at 0.8 % formulated in emulsion.
Melanin content was quantified with Fontana Masson staining.

Results: In skin explants melanin content was significantly boosted by 66%* vs placebo in a statistically significant manner, confirming the capacity of Neuroglow™ to promote pigmentation and skin protection.

Boosting melanogenesis in skin explants



Mann-Whitney test: *p<0.05

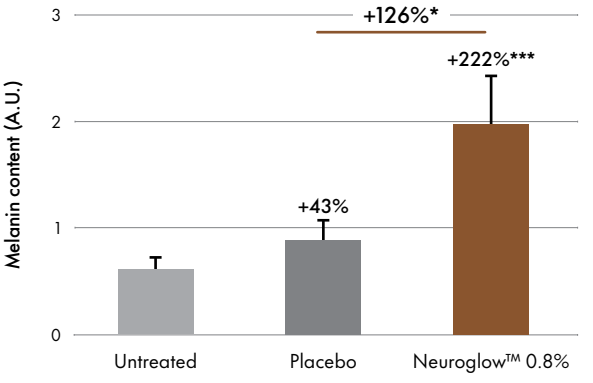
2. Neuroglow™ further boosts melanogenesis under daily light

Skin explants were topically treated for 5 days with an emulsion containing Neuroglow™ at 0.8% to prepare the skin, then they were UVA-B exposed twice on D4 and D5 in order to mimick daily exposure to solar radiation [4.5J UVA+0.15J UVB]. Melanin content was evaluated by Fontana Masson staining.

Results: A significant increase of melanin content was observed under irradiated condition showing +222%*** in comparison with untreated and up to +126%* in comparison with placebo.

A **boosting effect on melanin production** was observed with Neuroglow™ (**+126%** vs placebo).

Skin pigmentation activation



Mann-Whitney test: *p<0.05, ***p<0.001

3. Neuroglow™ changes skin glow/tone under day light

Pigmented Reconstructed Human Epidermis (RHE) (MelanoDerm™) were treated with Neuroglow™ at 0.8% in vehicle (Miglyol) for 14 days then they were UVA-B exposed twice on D9 and D13 in order to mimick daily exposure to solar radiation [4.5J UVA+0.15J UVB]. 24 hours later, RHE were collected and pictures were taken.

Results: In irradiated conditions, ITA parameter was -125%* compared to the placebo and L* parameter was -15%* compared to placebo (data not shown). This evidences the pro-pigmenting effect of Neuroglow™.

L* and ITA parameters decreased with Neuroglow™ in comparison to vehicle condition, evidencing a pro-pigmenting effect.

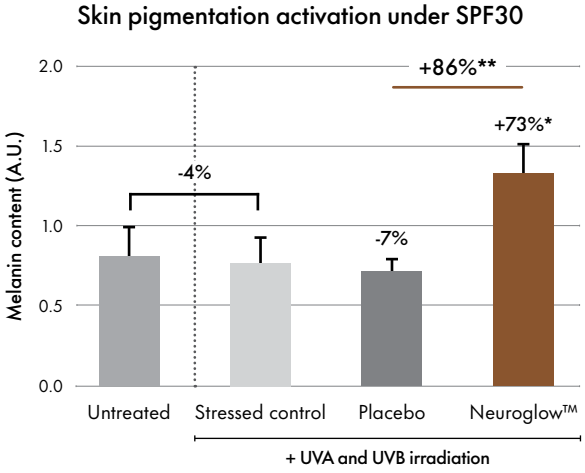
Biological activity

Neuroglow™ works with sun filters (SPF30)

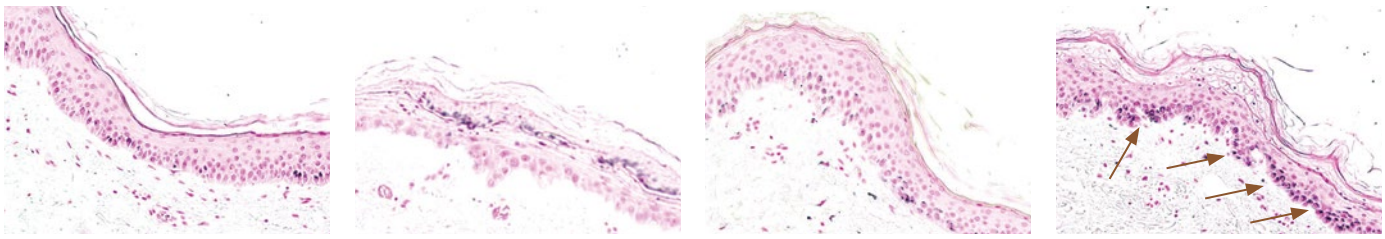
Ex vivo study with a SPF30 formula

Skin explants were treated with Neuroglow™ at 0.8% in sunscreen formula for 5 days and UVA-B challenged twice on D4 and D5 in order to mimic daily exposure [4.5J UVA + 0.15J UVB]. Melanin content was analysed by pigmentation index calculation following Fontana staining.

Results: In irradiated conditions with SPF formula, melanin content was boosted in the presence of Neuroglow™ by +86%**.
No pigmentation was noted with the placebo and irradiation conditions.



Mann-Whitney test: *p<0.05; **p<0.01



Untreated | Day light only | Placebo + day light | Neuroglow™ + day light

Neuroglow™ protects the skin: only the bright side of the sun

The downside of excessive sun exposure is that triggers skin inflammation, redness and erythema. Neuroglow™ was tested in a number of stressing conditions:

- chemical stress,
- heat stress to mimic sun burn conditions (IR-like),
- UVB stress to mimic sun.

1. Neuroglow™ protects against chemical stress mediated-inflammation

Keratinocytes were pre-treated for 24 hours with Neuroglow™ at 0.01%. A chemical stress (PMA 10ng/mL) was then induced. Cytokines release was then quantified in cell media after 24 hours of incubation using multiplex immunoassay.

Results: After chemical stress, Neuroglow™ has decreased the release of all pro-inflammatory markers : IL-6 by 45%*, IL-8 by 43%*, TNF-a by 44%* respectively vs placebo, indicating an anti-inflammatory and soothing effect.

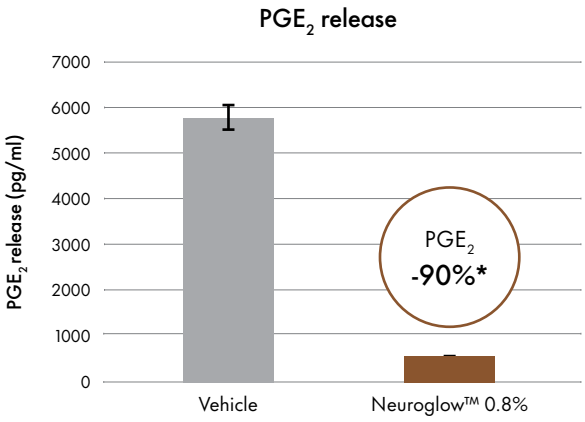
Mann-Whitney test: *p<0.05

2. Neuroglow™ protects against heat stress mediated-inflammation (IR-like)

Pigmented RHE were treated with Neuroglow™ at 0.8% in vehicle (Miglyol) for 14 days and a heat stress (5min at 60°C) at Day 9 and D13 mimicking sun burn was applied. Culture media were collected 24 hours after heat stress and PGE_2 was quantified using ELISA kit.

Results: In heat stress conditions, the release of the pro-inflammatory marker PGE_2 was inhibited on pigmented RHE by the treatment with Neuroglow™, up to **-90%***, suggesting a soothing effect after sun burn and from heat stress (IR-like) thanks to the downregulation of PGE_2.

Mann-Whitney test: *p<0.05

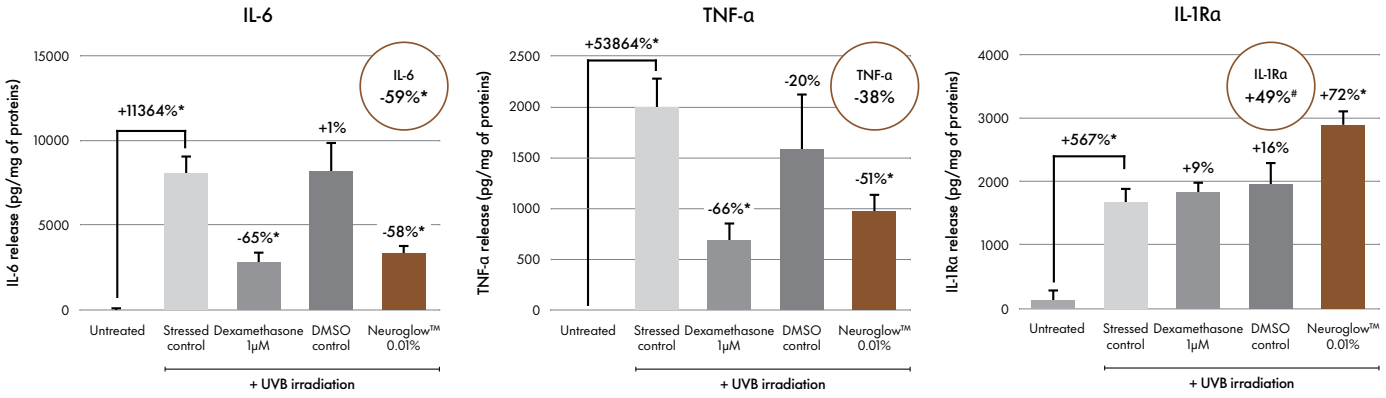


Neuroglow™ significantly inhibits inflammation (PGE_2) after heat stress, showing a soothing effect after sun burn.

Biological activity

3. Neuroglow™ protects against UVB stress mediated-inflammation

Keratinocytes were pre-treated for 24 hours with Neuroglow™ at 0.01%. Exposure to UVB at 75mJ/cm^2 was induced to mimic a sun burn. Cytokines release was then measured in supernatant after 24 hours of incubation by using multiplex immunoassay.



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

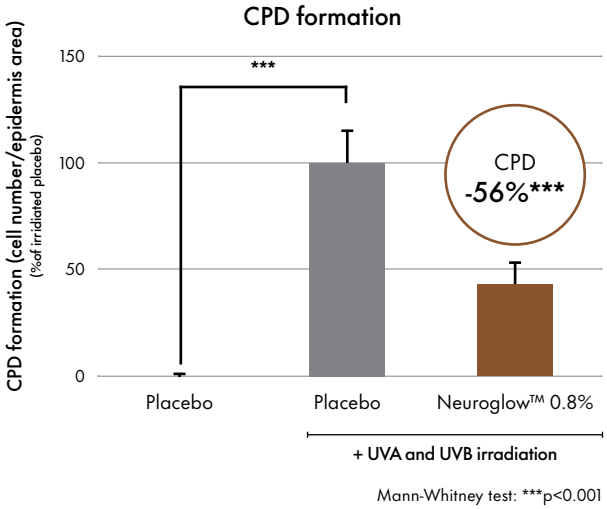
Results: In the sun burn model with UVB challenge, Neuroglow™ has modulated the release of all tested pro-inflammatory and anti-inflammatory markers: IL-6 by -59%* (vs vehicle) and by -58%* (vs untreated), TNF-α by -38% (vs vehicle) and by -51%* (vs untreated), IL-1Rα (anti-inflammatory) by +49%# (vs vehicle) and by +72%* (vs untreated), indicating an anti-inflammatory and soothing effect.

Neuroglow™ significantly increased the release of anti-inflammatory cytokine (IL-1Rα) and decreased pro-inflammatory cytokines (IL-6 and TNF-α) evidencing **soothing activity after sun burn.**

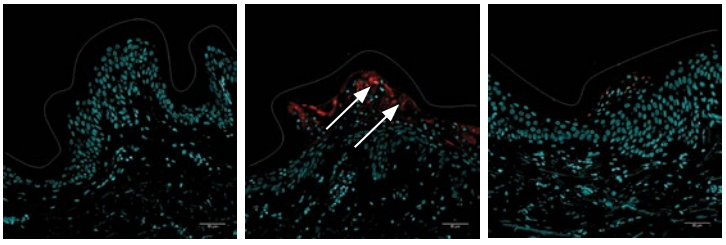
Neuroglow™ prevents ageing by protecting the skin DNA

UVB stress may trigger DNA damages, specifically promoting the formation of CPD (Cyclobutane Pirymidine Dimers): these small cycle dimers damage proper DNA replication and are considered as sun related-DNA damages.

Skin explants were treated for 5 days with Neuroglow™ at 0.8% in emulsion then UVA-B exposed twice at D4 and D5 in order to mimic daily exposure to solar radiation [4.5J UVA + 0.15J UVB]. CPD (DNA damages) were quantified by immunofluorescence detection.



Mann-Whitney test: ***p<0.001



Results: In the presence of pre-treatment with Neuroglow™, the formation of CPD was reduced by 56%*** vs placebo demonstrating a strong protection benefit.

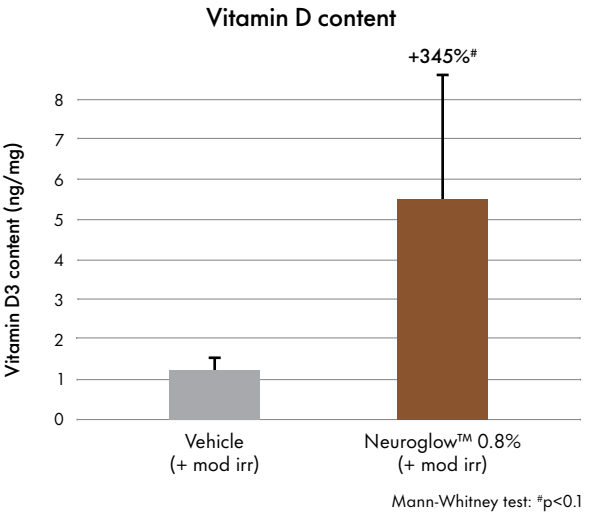
Neuroglow™ shows skin protection by reducing the formation of CPD (markers of DNA damage).

Biological activity

Neuroglow™ mimicks the healthy effects of sun

1. Stimulation of Vitamin D release in skin

The skin is responsible for producing Vitamin D, both in the epidermis and in the dermis; it has systemic functions when it enters blood flow (bone health, immune protection, mental health and cognitive performance, and inversely correlates to fatigue and blue mood); additionally Vitamin D in the skin increases barrier function, skin defense (by TLR2 activation and modulation of skin immune system) and protection of epidermal melanin.
Skin explants were treated with Neuroglow™ at 0.8% in vehicle (Miglyol) for 5 days and UVA-B exposed twice at D4 and D5 in order to mimic daily exposure to solar radiation [4.5J UVA + 0.15J UVB]. Then, one day later, skin explants were collected and Vitamin D was quantified by HPLC-LC/MS.

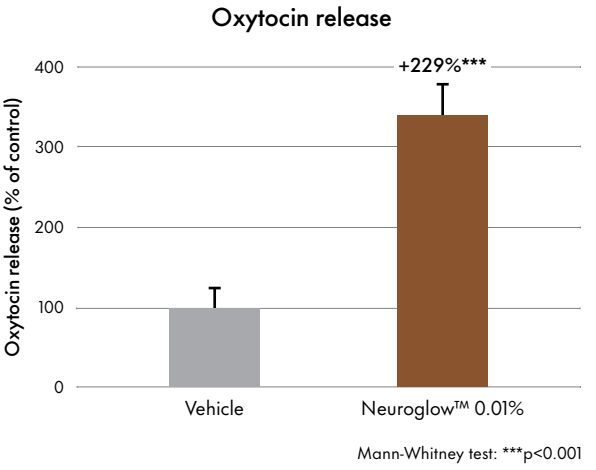


Results: In the presence of pre-treatment with Neuroglow™, **Vitamin D was boosted** by +345%# vs placebo in skin explants. Vitamin D boosting was also observed in the absence of irradiation by 86%# vs the control (data not shown) after 5 days in total of treatment with Neuroglow™ at 0.8%.

2. Boosting oxytocin, the "Love molecule"

Recent studies[5] report that oxytocin is found in the epidermis.
The oxytocin receptor represents a protective mechanism versus the release of pro-inflammatory cytokines.
In fact scientists have been able to correlate the release of oxytocin in the skin with skin ageing scores, suggesting a protective function in the epidermis in the case of sun exposure.

Keratinocytes were treated with Neuroglow™ at 0.01% in DMSO for 24 hours. At the end of the 24 hours' incubation period, oxytocin released in the supernatant was quantified using ELISA kit.

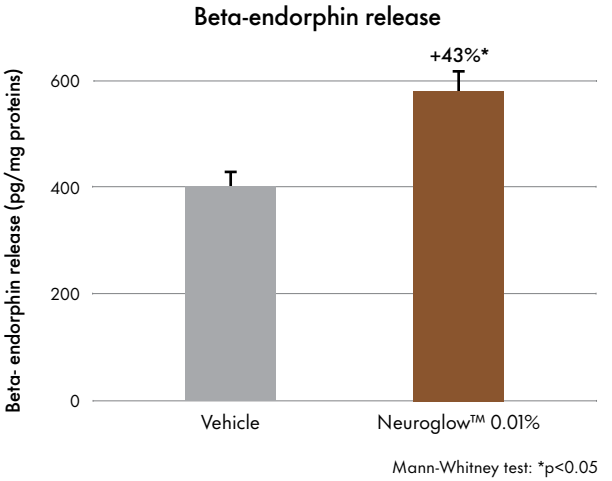


Results: Neuroglow™ **boosts the release of the molecule of love and bonding oxytocin** by +229%***.

3. Promoting the release of beta-endorphin for well-being

UV and sun light stimulate the release of beta-endorphin in the skin, which can create a general feeling of well-being.
Beta-endorphin can also promote the release of other hormones that are involved in feelings of well-being.

Keratinocytes were treated with Neuroglow™ at 0.01% in DMSO for 24 hours. At the end of the 24 hours' incubation period, beta-endorphin released in the culture medium was quantified using ELISA kit.



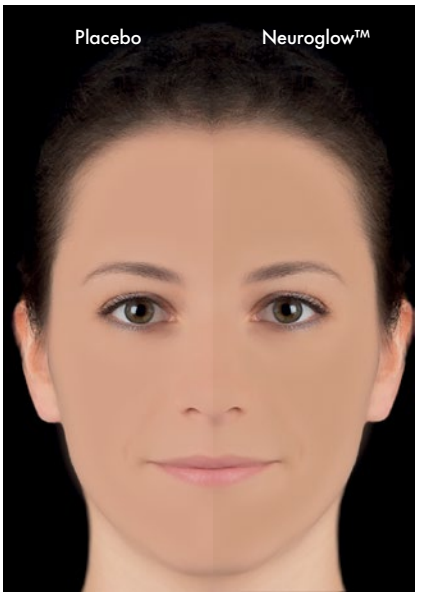
Results: Neuroglow™ **boosts the release of beta-endorphin**, the marker of well-being, by 43%*.

[5] Hayre N., 2020

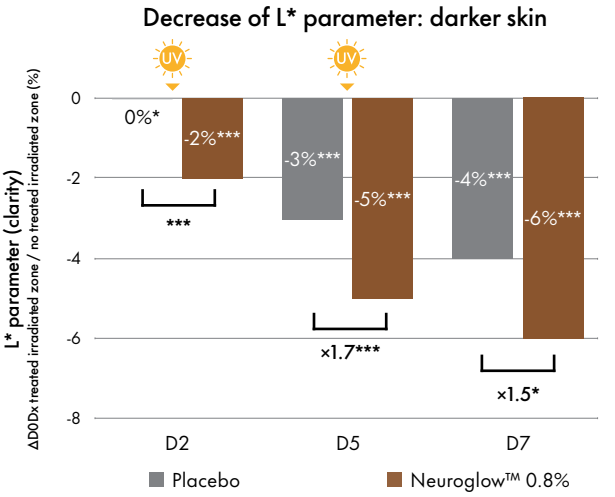
Clinical efficacy

Neuroglow™ boosts sun tanning (clinical study #1)

A panel of 22 women (aged from 18 to 59 years, average 35 y.o.) labelled as phototype II and III applied a cream containing Neuroglow™ at 0.8% as a pre-treatment over a week on their back (application by another person); they were then submitted to a 0.8MED[6] energy on D0, D2 and D5, representing sun tanning exposure.
The skin colour to evaluate Neuroglow™'s pro-pigmenting properties was evaluated on D0, D2, D5 and D7 based on the L* and ITA parameters (with a spectrophotometer).



AI generated image representing the skin colour measurements recorded on the back on D7.



Paired t test vs D0: *p<0.05, ***p<0.001

Results: In two days an equivalence of 3x difference was observed compared to the placebo for the L* parameter and a 2.5x difference, vs placebo, for the ITA parameter (data not shown). The observed pro-tanning was progressive from D2 to D7.

In 7 days, Neuroglow™ **induced a phototype shift in 76%*** of the volunteers, and of these, 40% shifted even to darker phototype IV (vs 0% in the placebo group).

ITA: Paired t test vs D0: *p<0.05, ***p<0.001

L*difference ×3

ITA difference 2.5× after **2 days** vs placebo

In **7 days** 76% of volunteers shifted from phototype II to phototype III

Neuroglow™ boosts well-being (clinical study #2)

1. Moodpict: energy and affection

A panel of 41 volunteers in total (women and men: 21 in the active group and 20 in the placebo group), aged 19 to 60 years, average 43 y.o., in winter blues condition (including blue mood, being gloomy and tired and sad due to lack of sun exposure, particularly during autumn and winter months) used a facial cream containing Neuroglow™ at 1.2% over 28 days (study started in January and ended in February in Europe).

Among several emotional universes proposed through suggestive images, the volunteers had to score, using a proposed scale, their perceived emotions felt (Moodpict questionnaire methodology).

Results: Neuroglow™ reduces the sense of tiredness by 26%* (vs placebo) and boosts the feeling of affection by +34%* (vs placebo).

Wilcoxon test vs D0: *p<0.05; **p<0.01 Mann-Whitney test vs placebo: *p<0.05

Tiredness **-26%***

Affection **+34%***

2. CES-D Questionnaire: good mood

The same panel was required to fill in a questionnaire (CES-D), one of the best known and widely used instruments in the field of mental health epidemiology. The CES-D scale is a short self-report scale designed to measure sad/blue condition in the general population.

Results: Neuroglow™ significantly improved the winter blues condition by 23%* vs placebo.
In the Neuroglow™ group, 81% reported a positive scoring on mood vs the placebo.

Wilcoxon test vs D0: *p<0.05, **p<0.01 Mann-Whitney test vs placebo: *p<0.05

Blue mood **-23%***

[6] MED (Minimal Erythemal Dose)=dose necessay to cause redness in a fair skinned person, approx 200-300J/m², equal to 2-3 SED; 1 SED /Stard Erythemal Dose) approx 100J/m²

Summary

Technical information

INCI:	Moringa Oleifera Seed Oil (and) Rosmarinus Officinalis (Rosemary) Leaf Extract (and) Polygonum Tinctorium Leaf/Stem Extract
Origin:	Green Fractionation
Preservation:	None
Appearance:	Pink oil – colour stability in oil [to sun test: 450W/m2 over 7h] [Temperature: 80°C over 8h]
Solubility:	Liposoluble
Dosage:	From 0.8% up to 1.2% for face and body care
Processing:	In emulsions Neuroglow™ can be added to the oily phase just before the emulsifying phase. If to be formulated in oils, it can be blended to the other oils at the end of the mixing.

Claims

Claims:	Healthy skin tanning stimulation, Skin tone and colour booster, Skin protection, Ageing prevention, Sun benefits mimicking, Tanning enabler and accelerator under day light, Skin preparation to sun exposure, Pigmentation enhancer, Skin tone darkener, Melanin booster, Skin health booster, Winter blue sadness reverser due to lack to sunlight exposure, Well-being enhancer.
Applications:	Body care, Facial care, Sun care (Sun prep., After sun, in combination with SPF), Products targeting well-being, Mimicking all the benefits of the sun.

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Givaudan

Human by nature

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