



BLUSH OLÉOACTIF®

Make peace with sensitive skin

Substantiated oil-based active ingredient concentrated by
Oléo-éco-extraction patented green process

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BLUSH OLÉOACTIF®

FORGET ABOUT SKIN SENSITIVITY AND SEE 'LA VIE EN ROSE'

Concerns about skin sensitivity have gradually increased due to worsening environmental pollution, climate change and a sustained need to wear masks. BLUSH Oléoactif® is a 100% natural liposoluble active inspired by the ancestral use of an indigo-plant: *Persicaria tinctoria*, sourced from European organic fields. It provides quantifiable benefits versus a placebo by enhancing not only skin condition (redness, complexion and comfort), but also consumers' self-perception and emotional state.

A DYEING PLANT WITH HEALTH BENEFITS

Persicaria tinctoria has been used by dyers since ancient times to produce indigo dye which is considered the oldest natural dye in the world. It is obtained through a fermentation process of *Persicaria* leaves which lasts several days. When submitted to successive macerations in water, decantations and filtrations, the green leaves give birth to a dark-blue powder and a key compound, indirubin, is synthesized. In nature, this secondary metabolite is secreted by the plant in conditions of stress due to physical wounds, disease, or attack by insects or fungi.



INDIRUBIN'S DUAL EFFECT ON EPIDERMIS

We know that sensitive skin is characterized by an alteration of the skin barrier, leading to Trans Epidermal Water Loss (TEWL) that may promote transcutaneous penetration of irritants such as pollutants and UVs, which in turn trigger inflammatory disorders. That is why our challenge is to find a phytocompound that is capable of both reducing keratinocytes pro-inflammatory response and protecting the skin barrier. Indirubin offers this perfect combination. Its activity on the skin is well documented. It acts:

- On skin's physical barrier to reduce inflammatory lesions^{1,2,3,4}, restore an optimal balance between keratinocytes proliferation and differentiation^{1,2,3}, and repair the tight junctions which play a crucial role in skin barrier integrity⁵,
- On the immune barrier through the modulation of inflammation (cytokines release, NO, IgE, ...) ^{6,7,8,9}.

Using our unique, eco-friendly Oléo-éco-extraction technology, the biological activity of the beautiful, pinkish-red indirubin molecule can be assessed efficiently.

ALLEVIATES THE WARNING SIGNS OF SENSITIVE SKIN

Keratinocytes are not only static bricks of the epidermal wall but cells that are immunologically active and critically involved in skin inflammation. They act as sensors of danger and producers of IL-1 α which can be considered as a skin alarm, also called 'Alarmin.' It functions as a danger signal to cellular damage due to inflammation, allergens, or ROS (among others). An ex vivo test is conducted to evaluate IL-1 α secretion following two types of environmental aggressions: pollutants and UVs. Skin explants are topically pretreated with 3 applications of 1% of BLUSH Oléoactif® or left untreated. IL-1 α immunostaining and a subsequent image analysis allow us to visualize and quantify the IL-1 α fixed on skin tissues. IL-1 α is visibly decreased when the skin is treated with BLUSH Oléoactif® (-29%* vs control).



BLUSH Oléoactif® relieves the inflammatory response of Alarmin IL-1 α .

¹ Yin-Ku Lin and al., Anti-psoriatic effects of indigo naturalis on the proliferation and differentiation of keratinocytes with indirubin as the active component. Journal of Dermatological Science 54 (2009) 168–174.

² Mi Hye Kim and al., Indirubin, a purple 3,2-bisindole, inhibited allergic contact dermatitis via regulating T helper (Th)-mediated immune system in DNCB-induced model. Journal of Ethnopharmacology 145 (2013) 214–219.

³ Ken Miyoshi and al., Attenuation of psoriasis-like skin lesion in a mouse model by topical treatment with indirubin and its derivative E804. Journal of Dermatological Science 65 (2012) 68–76.

⁴ Y.-K. Lin and al., Comparison of indirubin concentrations in indigo naturalis ointment for psoriasis treatment: a randomized, double blind, dosage-controlled trial. British Journal of Dermatology (2018) 178, pp124–131.

⁵ Yin-Ku Lin and al., Indigo naturalis upregulates claudin-1 expression in human keratinocytes and psoriatic lesions. Journal of Ethnopharmacology 145 (2013) 614–620.

⁶ Jinyoung Lee and al., Anti-inflammatory activity of *Persicaria tinctoria* extract against the environmental toxic stress-induced inflammation in HaCaT keratinocytes. Natural Products Science College of Pharmacy The Graduate School Seoul National University (2016).

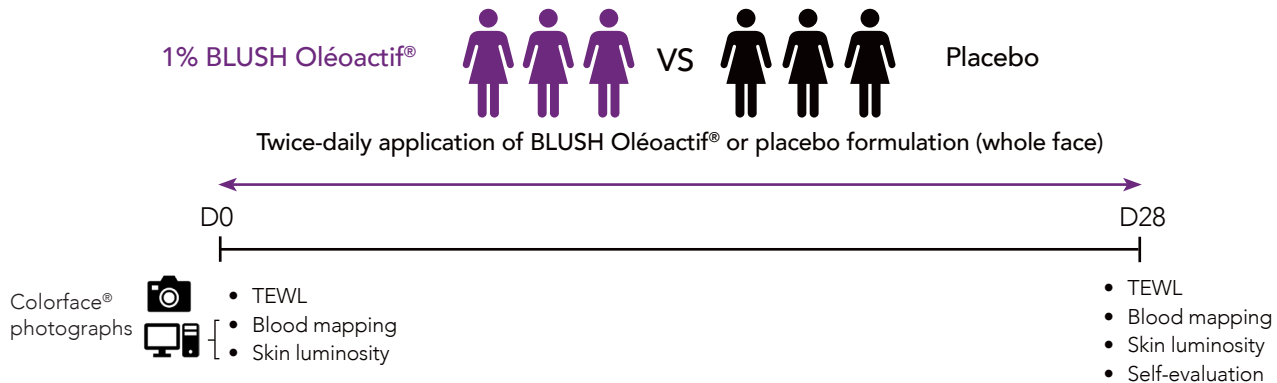
⁷ Tatsuya Ishihara and al., Polygonum tinctorium extract suppresses nitric oxide production by activated macrophages through inhibiting inducible nitric oxide synthase expression. Journal of Ethnopharmacology 72 (2000) 141–150.

⁸ Mi Hye Kim and al., Indirubin, a purple 3,2-bisindole, inhibited allergic contact dermatitis via regulating T helper (Th)-mediated immune system in DNCB-induced model. Journal of Ethnopharmacology 145 (2013) 214–219.

⁹ Toshio Kunikida and al., Indirubin inhibits inflammatory reactions in delayed-type hypersensitivity. European Journal of Pharmacology 410 (2000) 93–100.

CLINICALLY TESTED ON PEOPLE HAVING SENSITIVE SKIN AND WEARING MASKS DAILY

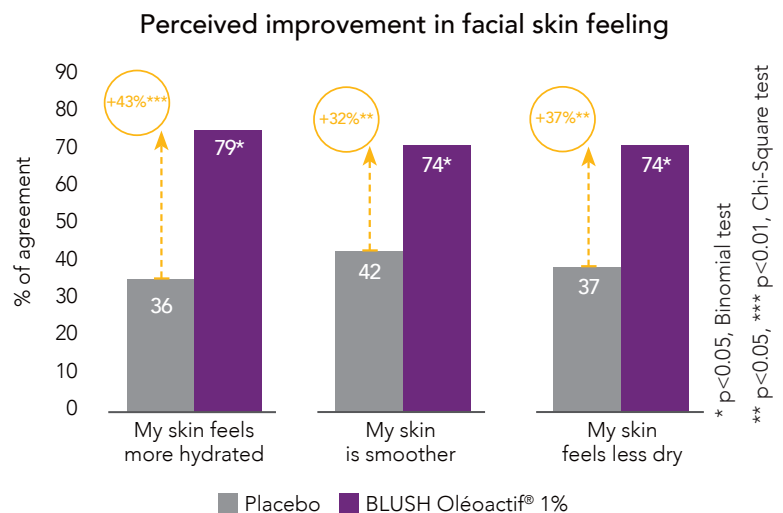
The effects of BLUSH Oléoactif® at 1% dose are also evident *in vivo*. A double-blind randomized study is performed on 40 women aged between 30 and 50 years old, separated into two distinct groups. All of them have sensitive skin with permanent facial redness and wear daily a facial mask (average 6 hours a day).



Protects skin barrier

Environmental factors, lifestyle, emotions, stress and mask-wearing increase skin fragility and affect its protective barrier. In this study, TEWL assessment is performed on volunteers with sensitive skin who wear a face mask every day for an average of 6 hours, which is a highly aggressive situation for the skin. The results show a significant increase of TEWL over time of +17% ($p < 0.001$ compared to D0, Student's t-test) for the subjects who used the placebo, while with the BLUSH Oléoactif® formulation, the TEWL level after 28 days of use does not evolve significantly. The decrease of water loss compared to the placebo reflects the overall protection of the skin barrier. This protective effect is associated with volunteers' positive perceptions. Their skin feels more hydrated, smoother, and less dry with statistically significant increases versus placebo of respectively +43%***, +32%** and +37%**.

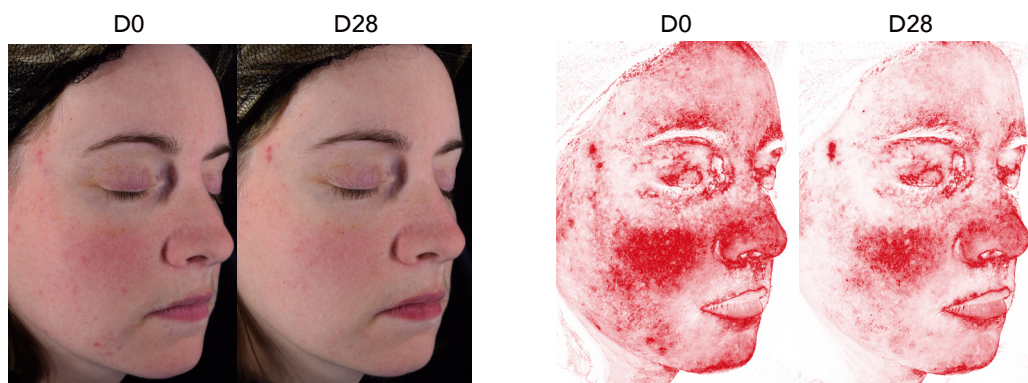
Furthermore, a significant majority of them perceive that their skin feels more comfortable.



Self-perceived efficacy of BLUSH Oléoactif® vs placebo at D28

Visibly reduces redness

The visible effect of increased vasodilatation due to the release of pro-inflammatory mediators (i.e., IL1- α , NO) is redness. The effect of BLUSH Oléoactif® on this parameter is evaluated. High resolution facial photographs in cross polarized light to visualize the changes in skin color are taken using ColorFace®. The use of a dedicated software allows us to determine the hemoglobin image (also called 'blood map') to demonstrate the effects of BLUSH Oléoactif® treatment on vascular redness.



Evaluation of reduction of redness at D0 and D28 (Colorface®) in Vol no.13 - 38 years old - daily mask wearing 8 hours per day

BLUSH Oléoactif® visibly reduces redness contrary to placebo.

The redness is reduced by 4 times compared to placebo, and up to -30% for the best volunteer.

Promotes healthy-looking skin

The appearance of unhealthy skin can have serious negative consequences on well-being. Skin complexion is therefore an important parameter to consider. High resolution photographs with ColorFace® in diffuse light are taken. Luminosity is quantified by image analysis. After 28 days, BLUSH Oléoactif® clearly outperforms the placebo by increasing the luminosity level of the skin by 5 times ($p < 0.05$ compared to placebo, Student's t-test). A statistically significant majority of volunteers perceives this improvement in their complexion with their skin feeling brighter, less tired, and healthier.



Evaluation of skin luminosity at D0 and D28 (Colorface®) in Vol no. 13 - 38 years old - daily mask wearing 8 hours per day

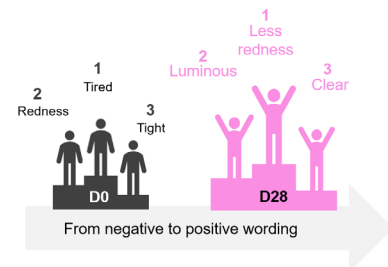
EMOTIONALLY APPROVED BY PEOPLE SUFFERING FROM SENSITIVE SKIN

What if these improvements in sensation and clinical signs of sensitive skin could bring positive emotional benefits? This is precisely what has been demonstrated thanks to an expert laboratory through a specific method called Mirror Test™. This emotional assessment is performed in a double-blind randomized study versus placebo. All subjects are aged between 30 and 50 years old, and have sensitive skin with redness. This test consists of confronting the volunteers with their reflection in the mirror, which is a highly emotional situation. Then, three open questions are orally asked:



- How do you perceive yourself physically?
- How have you been feeling these last few days?
- How do you feel about the condition of your skin?

A full audio recording of spontaneous answers is carried out using a hidden microphone. Then subjects' verbatim responses are submitted to a quantitative statistical analysis:



Placebo

Terms at D0		Terms at D28	
Pimples	$p = 0.029$	Good	$p = 0.002$
Oily	$p = 0.032$	Smoother	$p = 0.006$
Red	$p = 0.043$	Improved	$p = 0.011$

1% BLUSH Oléoactif® formulation

Terms at D0		Terms at D28	
Tired	$p = 0.028$	Less redness	$p = 0.011$
Redness	$p = 0.037$	Luminous	$p = 0.034$
Tight	$p = 0.049$	Clear	$p = 0.049$

All terms are statistically significant according to the Factorial Analysis of Correspondence. Frequency of appearance significant $p < 0.05$

Verbal responses significantly evolve over time for both products. Nevertheless, the terms used are different. Terms associated with BLUSH Oléoactif® formulation at the beginning of the study are: tired, redness and tight. They are predominantly associated with negative terminology. At D28, a more positive terminology stands out with words like less redness, luminous and clear. These results completely corroborate the results of the first *in vivo* study.

BLUSH Oléoactif® improves, at clinical level, skin condition, general emotional state and self-perception when used at 1% in a formula versus placebo.

TECHNICAL AND REGULATORY DATA

INCI NAME:	Brassica Campestris (Rapeseed) Seed Oil (and) Polygonum Tinctorium Leaf Extract
RECOMMENDED DOSE:	1% - 5%
RECOMMENDED pH:	3-10
SOLUBILITY:	Liposoluble
FORMULATION:	In the fatty phase before emulsification or at the end of the formulation process or directly in anhydrous formulas.
APPLICATIONS:	Skin care for sensitive and reactive skin, positive ageing, urban skin care; face serum, beauty mask, make-up, anhydrous formula, natural and organic product, rosy shades.



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