# Sunshine in a Bottle: Harnessing the Power of *Persicaria tinctoria* Extract for Radiant Skin and Enhanced Well-being

M. De Tollenaere, A. Durduret, E. Chapuis, J. Martinez, B. Sennelier-Portet, A. Scandolera, R. Reynaud

**abstract**

Givaudan Active Beauty has developed an ingredient derived from *Persicaria tinctoria*, a botanical species of the buckwheat family, with the purpose of replicating the positive effects of sunlight. This innovative extract is designed to promote well-being and stimulate tanning without the need for actual sun exposure. Its main focus is to address the mood changes that occur during seasonal transitions, particularly in winter, when there is limited sun exposure and lower levels of vitamin D3. Givaudan conducted extensive research using *in vitro* models of keratinocytes and melanocytes that were co-cultured and *ex vivo* models to evaluate the pro-pigmenting activity. β-endorphin and oxytocin were quantified in the culture medium of keratinocytes stimulated with the extract. Vitamin D3 production was measured after the grinding of skin explants treated for several days with *Persicaria tinctoria* extract.

Finally, clinical trials were conducted to demonstrate the extract's ability to enhance mood and improve skin health. Corroborating the hypothesis that the extract can act as a "molecular sun", the results demonstrated its ability to significantly increase melanin content up to +66% in skin explants in comparison with placebo cream. In keratinocytes stimulated with the extract, β-endorphins increased by +43% and oxytocin by +229%. Vitamin D3 production rose significantly to 86.5%. A positive effect on mood was confirmed *in vivo* in a panel of volunteers who fill specific questionnaires and said they observed a significant reduction of tiredness and an increase of affectionate mood state, leading to an overall improvement of low mood.

In summary, *Persicaria tinctoria* extract offers myriad of sun-mimicking benefits including tanning activity, mood-enhancement and vitamin D3 stimulation. This can help address vitamin D deficiency and support overall skin and body health, particularly in regions and seasons with limited sunlight.

## Introduction

The beneficial effects of the sun, including the production of β-endorphin, vitamin D3, and melanin synthesis, are well-documented[1,2]. Vitamin D3 plays a crucial role in skin barrier function, immune defense, and overall health, with individual differences in vitamin D3 production influenced by age, gender, and skin type [3,4,5,6,7,8]. Ultraviolet radiation (UVR) generated by the sun not only stimulates melanin synthesis for skin tanning [9], but induces the release of β-endorphins, an endogenous opioid, which contributes to feelings of well-being by reducing cortisol [1,10]. Additionally, exposure to the sun may produce oxytocin, a feel-good hormone associated with social bonding that is also described as a soothing molecule [11,12].

However, seasonal changes, particularly during winter, can lead to mood changes, including a feeling of low mood or "winter blues", creating a high desire for sun-seeking behaviour to recover these beneficial effects [1,10].

Givaudan Active Beauty dedicates its research to developing natural ingredients that provides well-being. In this context, Givaudan pushed the boundaries by developing an ingredient capable of mimicking the positive effects of the sun. Researchers crafted an extract from *Persicaria tinctoria*, a botanical species of the buckwheat family, also known as Japanese Indigo [13,14]. The goal was to promote well-being and induce tanning without sun exposure, thus addressing seasonal mood changes that come from a lower exposure to the sun and to vitamin D3.

The research sought to mimic the myriad benefits of sunlight exposure and vitamin D3 production to stimulate improved overall health and well-being. To demonstrate the efficacy of the extract in enhancing mood and skin health, Givaudan employed *in vitro* and *ex vivo* models, along with a clinical trial.

## Materials and methodology

### Evaluating pro-pigmenting activity *in vitro*

Normal Human Keratinocytes (NHKs) were initially seeded in 6-well plates pre-coated with collagen I. After 24 hours, Normal Human Melanocytes (NHMs) were seeded into the same 6-well plates. The cells were cultured for 48 hours in complete medium (Dermalife supplemented with factors, Cell Systems, LL-0007) at 37°C with 5% $CO_2$. Following the 48-hours in-

cubation period, the cells were stimulated for five days with either the pro-pigmenting control (L-tyrosine (Sigma-Aldrich, T1145) at 450µg.mL$^{-1}$ and α-MSH (Sigma-Aldrich, M4135) at 1nM) or with the *Persicaria tinctoria* extract at 0.01% (Neuroglow™, Givaudan). Untreated cells were left as the control condition. Treatments were renewed every other day. After five days of treatment, cells were rinsed with PBS and melanin was extracted using 0.5N NaOH. Optical density was measured at 405 nm with a microplate reader (TECAN SPARK® 10M).

### Evaluating pro-pigmenting activity on skin explants using Fontana Masson's staining

Skin explants, obtained with the informed consent from the abdominal surgery of a 37-year-old female Caucasian donor were cultured on metal grids into standard 12-well plates in DMEM medium (high glucose, (4.5g/L), supplemented with glutaMAX and Fetal Bovine Serum (FBS) (10%) and Penicillin-Streptomycin (1%) at 37°C with 5% $CO_2$. The culture medium was renewed every 24 hours. The skin explants were topically treated with *Persicaria tinctoria* extract formulated in emulsion (INCI below) at 0.8%, compared to a placebo cream and an untreated condition. Treatments and medium were renewed daily for five days. After five days of stimulation, the cream was removed from the surface and each explant was cryopreserved in OCT and stored at -80°C until further processing. Explant sections (5 µm thick) were obtained using a cryostat (Leica) and fixed with a solution containing 95% ethanol and 5% acetic acid. Fontana-Masson staining (Sigma-Aldrich) was conducted following the provider's protocols. The images were collected with a microscope (Evos M5000, Thermo Fisher) at a resolution and exposure settings with a 40x objective, and analysed with ImageJ software (Schneider, 2012). For each experimental group, the melanin index was determined by integrating the stained areas at the stratum basale level, normalized against the control group to obtain a percentage of occupancy.

INCI formula:
AQUA/WATER, CETYL ALCOHOL, GLYCERYL STEARATE, PEG-75 STEARATE, CETETH-20, STEARETH-20, ISODECYL NEOPENTANOATE, PHENOXYETHANOL ±PERSICARIA TINCTORIA EXTRACT, DIMETHICONE, FRAGRANCE

### Enhanced positive mood and well-being: Quantifying beta-endorphin release in keratinocytes

Normal Human Epidermal Keratinocytes (NHEKs) were seeded in a type I collagen pre-coated 24-well plate. After reaching confluency, the NHEKs were treated for 24 hours with Amantadine hydrochloride at 0.1µM as a positive control for beta-endorphin release activator, with *Persicaria tinctoria* extract at 0.01% (v/v). Following 24 hours of incubation, the cell media were collected and frozen at -20°C before analysis. Cell lysates were extracted and the proteins contained in the cell lysates were quantified using a spectro-colorimetric method (Thermo-Scientific Pierce Bradford™ Protein Assay Kit). The presence of beta-endorphins in the cell media was assessed using the beta Endorphin ELISA kit (catalogue no. ABIN6963481).

### Enhancement of positive mood and well-being: Quantifying oxytocin release in keratinocytes

Normal Human Epidermal Keratinocytes (NHEKs) were seeded in a type I collagen pre-coated 24-well plate. The cells were incubated for 48 hours in complete medium (Dermalife supplemented with factors, Cell Systems, LL-0007) and 1% of antibiotics (Sigma-Aldrich) at 37°C with 5% $CO_2$. After the incubation period, the cells were rinsed twice with PBS (Gibco) and pre-incubated with *Persicaria tinctoria* extract at 0.01% (v/v) for 24 hours in a Dermalife basal medium with 1% of antibiotics at 37°C with 5% $CO_2$. Following 24 hours of pre-incubation, the cell media were collected and centrifuged at 2000g for 10 minutes at 4°C to eliminate dead cells. The media were

then stored at -20°C. An MTT assay was performed to evaluate treatment toxicity and the normalisation of oxytocin quantification. Oxytocin was quantified using the ELISA kit ADI-900-153A-0001 (Enzo Life Sciences).

### Enhanced positive mood and well-being: Quantifying vitamin D3 in skin explants

Skin explants were obtained with informed consent from breast and abdominoplasty surgeries from 54-year-old and 50-year-old female donors. The explants were kept viable by culturing them on biocompatible plastic grids in standard 24-well plates in an air-liquid interface with skin a culture medium (Givaudan) at 37 °C with 5% $CO_2$. The culture medium was renewed every 24 hours. Skin explants were topically treated either with the *Persicaria tinctoria* extract diluted at 0.8% in Miglyol 812® or just with Miglyol 812® as a vehicle control. After five days of incubation, the surfaces of the skin explants were rinsed with PBS, then frozen at -80°C for storage before further investigation. Vitamin D3 was extracted from the skin explants using methanol and measured using the High-Performance Liquid Chromatography (HPLC) method.

### Clinical evaluation of the mood-boosting properties of *Persicaria tinctoria* extract

A clinical study was carried out on 41 male and female volunteers aged between 18 to 58 years, with an average age of 43 ±13 years old. Participants were divided into two groups; a group of 21 volunteers comprising 11 women and 10 men, who applied the active cream; and a second group comprising 11 women and 9 men, who applied the placebo formula. The volunteers were recruited on the basis of their ability to match the inclusion criteria; this included having a skin phototype between I to III, and a tendency to experience tiredness or the "winter blues" due to a lack of sun exposure. Volunteers applied a cream twice a day for 28 days, either containing 1.2% of *Persicaria tinctoria* extract or a placebo. After 28 days, the volunteers' well-being was analysed using a Moodpict questionnaire and a short self-report depression scale (CES-D). The clinical study took place in Barcelona, between January and February, when the city experiences very low sun exposure.

The study was conducted in accordance with the Declaration of Helsinki and the protocol was reviewed and approved by the Givaudan Internal Review Board, with the protocol number 2023-002.

INCI formula:
AQUA/WATER, CETHYL ALCOHOL, GLYCERYL STEARATE, PEG-75 STEARATE, CETETH-20, STEARETH-20, ISODECYL NEOPENTANOATE, PHENOXYETHANOL, ± PERSICARIA TINCTORIA EXTRACT, DIMETHICONE, AND FRAGRANCE.

## Results

### Sun-like effects of *Persicaria tinctoria* extract

To evaluate the efficacy of *Persicaria tinctoria* extract and its ability to enhance melanogenesis, Givaudan conducted a study using a co-culture of keratinocytes and melanocytes. The cells were exposed either to the pro-pigmenting control containing L-tyrosine and α-MSH, two well-known melanogenesis stimulators, or to *Persicaria tinctoria* extract at 0.01%. The purpose of the study was to assess the performance of the active ingredient under basal conditions, without additional stimulants. As **Figure 1** shows, the study found that melanin levels in cell lysates significantly increased following stimulation by the pro-pigmenting control, indicating the culture's responsiveness (+51%*). Quantification of melanin after treatment with 0.01% Persicaria tinctoria extract revealed a +30%* increase in comparison to the untreated condition, demonstrating the pro-pigmenting activity of the ingredient.

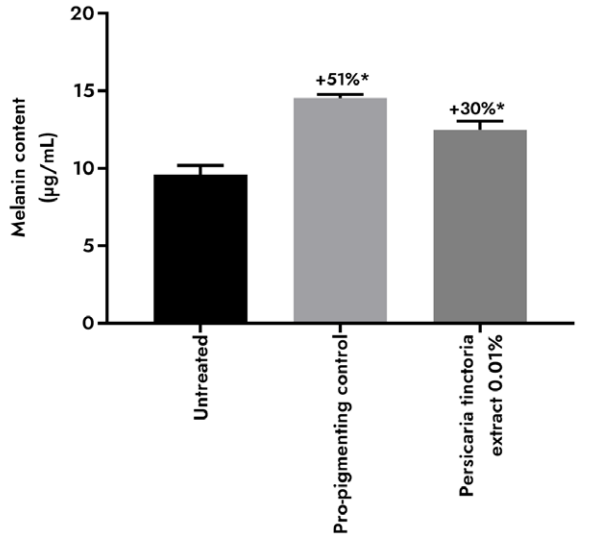


**Fig.1** Melanin quantification in cell lysates of co-culture of keratinocytes and melanocytes. Statistical significance is calculated using Mann-Whitney test with * p<0.05.

After demonstrating the pro-pigmenting effect of *Persicaria tinctoria* extract on the co-culture, these findings were validated using a more physiologically relevant model, namely skin explants. Through Fontana- Masson staining, a significant increase in melanin content in the skin was observed, with Persicaria tinctoria extract at 0.8% displaying a remarkable enhancement of +66% melanin content compared to the placebo cream which demonstrated only a modest effect on skin pigmentation at +9% **(Figure 2)**. These findings confirm the pro-pigmenting activity of Persicaria tinctoria extract in an *ex vivo* model. Validating this effect, on skin explants provides a robust model for evaluating enhancements in melanin synthesis.

Further experiments explored the presence of well-being molecules and showcased significant enhancements in β-endorphin and oxytocin release in keratinocytes treated with *Persicaria tinctoria* extract compared to controls.

Studies demonstrated robust responsiveness of the model as evidenced in the significant stimulation of β-endorphin release (+71%*), by the positive reference of Amantadine hydrochloride at 0.1µM **(Figure 3)**. Under the same experimental conditions, the DMSO control induced a non-significant release of β-endorphin by +30%, while *Persicaria tinctoria* extract significantly stimulated its release by +86%* compared to an untreated condition, and by +43%* compared to the vehicle control (DMSO).

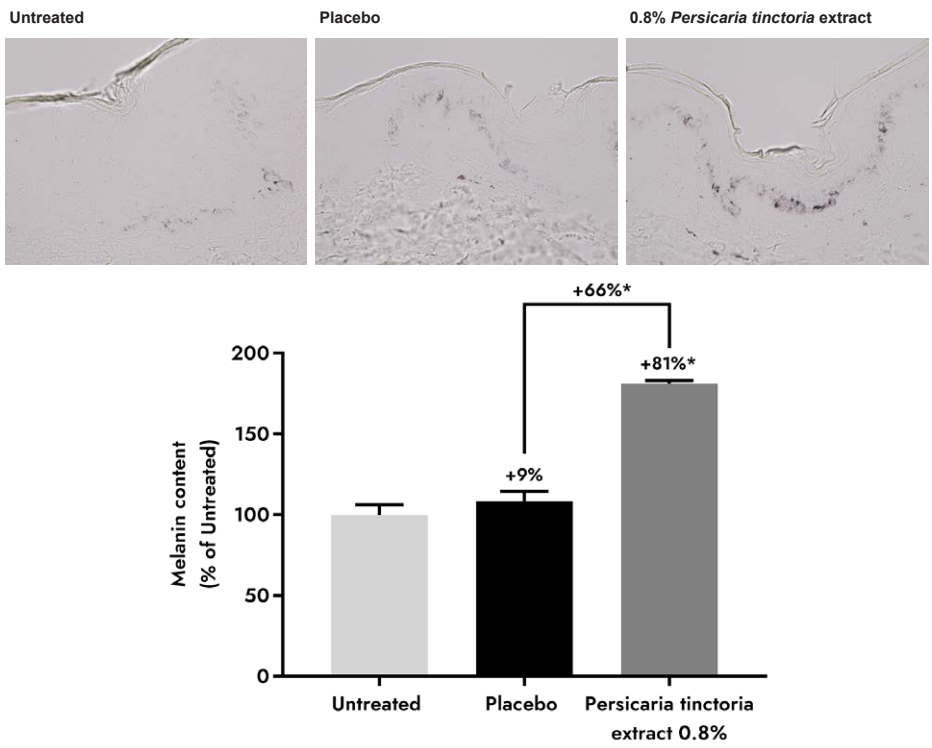


**Fig. 2** **(Top)**: Pictures of skin slices stained with Fontana Masson staining after five days of treatment with 0.8% *Persicaria tinctoria* extract showing melanin content in the skin. **(Bottom)**: Quantification of melanin content in the skin by image analysis. Statistical significance is calculated using Mann-Whitney test with * p<0.05.

In keratinocytes, the release of oxytocin was measured following 24 hours of treatment with *Persicaria tinctoria* extract or its vehicle (DMSO).

**Figure 4** shows that *Persicaria tinctoria* extract significantly stimulated the release of oxytocin by +229%*** compared to its vehicle (DMSO).

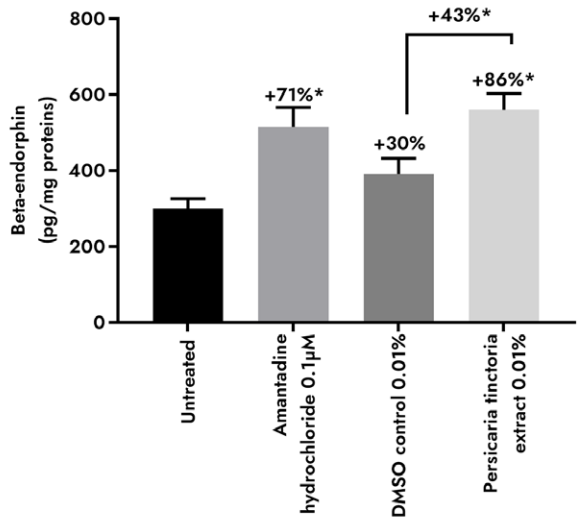


**Fig. 3** Beta-endorphin quantification in keratinocytes supernatant treated for 24 hours with Amantadine hydrochloride (positive reference), *Persicaria tinctoria* extract diluted at 0.01% in DMSO and DSMO only. Statistical analysis with Mann-Whitney test with * p<0.05.

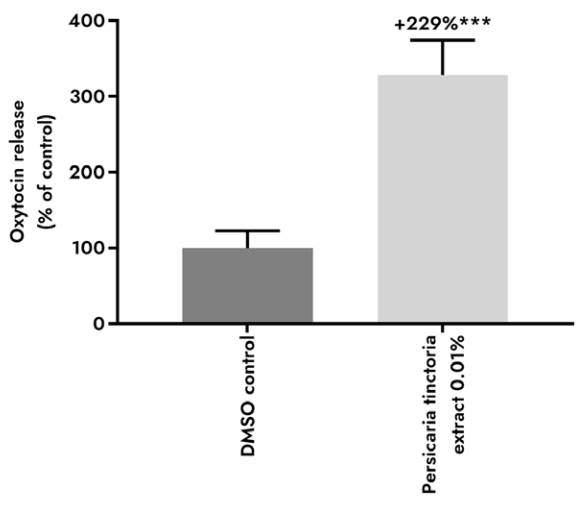


**Fig. 4** Oxytocin quantification in keratinocytes supernatant treated for 24 hours with *Persicaria tinctoria* extract diluted at 0.01% in DMSO and DSMO only. Statistical analysis with Mann-Whitney test with * p<0.05.

Finally, the study analysed the production of vitamin D3 in skin explants, a well-being effector correlated to sun exposure. It was observed that a repeated application of *Persicaria tinctoria* extract significantly induced the production of vitamin D3 by +86.5%# in comparison to the vehicle control, demonstrating a positive impact on this well-being mediator even without the presence of sunlight **(Figure 5)**.

In summary, based on the findings, **it can be affirmed that *Persicaria tinctoria* extract significantly exerts a sun-like effect by enhancing the production of vital well-being and healthy effectors such as β-endorphin and vitamin D3**. Furthermore, *Persicaria tinctoria* extract stimulated the release of oxytocin, the "molecule of love", and provided a well-being effect.

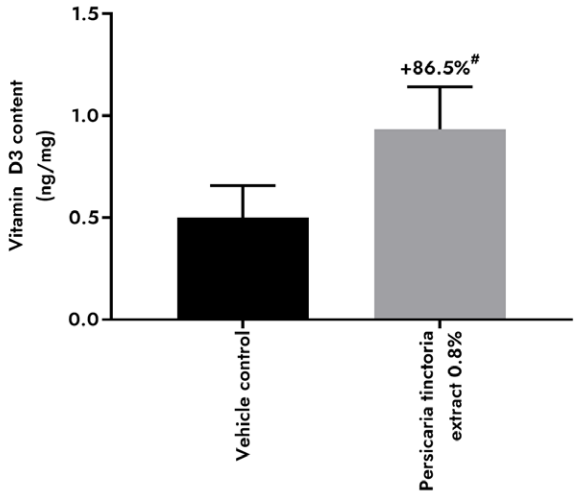


**Fig. 5** Vitamin D3 quantification in skin explants treated or untreated with *Persicaria tinctoria* extract at 0.8%. Statistical analysis with Mann-Whitney test with # p<0.1 and * p<0.05.

## Clinical study on mood-enhancement

A clinical study was carried out on men and women experiencing low moods due to a lack of sun exposure during winter. Volunteers applied the extract formulated in a cream at 1.2% twice daily for 28 days while another group used a placebo. Evolution of tiredness and mood was evaluated after this period. Results showed that the extract was able to significantly reduce tiredness by -40% in comparison to baseline (D0) while the placebo only reduced fatigue by -14. Notably, the active ingredient showed a significant improvement in tiredness and mood compared to the placebo, with a reduction of -26%.

## Tiredness reduction, improved mood and improved feelings of affection

In addition, affectionate moods were studied, due to the finding that *Persicaria tinctoria* extract is able to stimulate oxytocin release *in vitro*. It was found that the active ingredient at 1.2% is able to significantly increase an affectionate mood state by +32% compared to the initial state (D0), while the placebo led to a slight reduction of -2%.

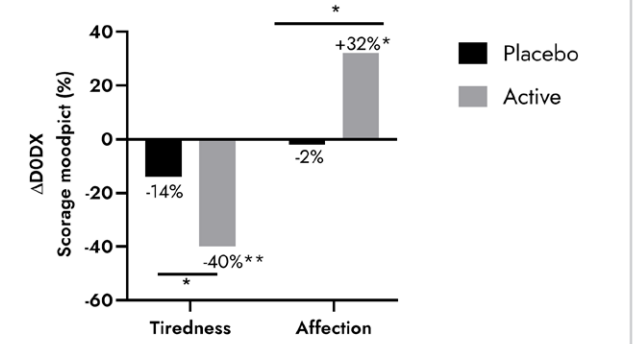


**Fig. 6** Evolution of tiredness and affectionate mood after 28 days of twice daily application of cream containing 1.2% of active or placebo by using Moodpict questionnaire. Statistical analysis with Wilcoxon and Mann Whitney test with * p<0.05 and ** p<0.01.

After 28 days the active ingredient demonstrated significant superiority over the placebo with a significant increase in affectionate mood of +34% **(Figure 6)**. These findings show that Persicaria tinctoria extract is able to significantly trigger well-being benefits by reducing tiredness and increasing an affectionate mood.

Using a questionnaire, the study analysed individuals experiencing a low mood due to a lack of sun exposure during winter. Findings showed that the active ingredient at 1.2% significantly reduced low mood by -42% compared to the D0, while a placebo decreased a low mood by -19%, but in a non-significant manner **(Figure 7)**. The active ingredient showed a significant -23% reduction compared to the placebo.

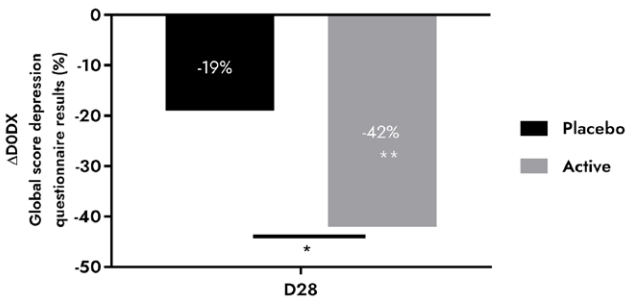


**Fig. 7** Evolution of negative mood after 28 days of twice daily application of cream containing 1.2% of active or placebo by using CES-D methodology. Statistical analysis with Wilcoxon and Mann Whitney test with * p<0.05, ** p<0.01.

## Discussion

This study assessed the efficacy of *Persicaria tinctoria extract* in promoting skin health and well-being and yielded several key findings across skin physiology and mood regulation.

Firstly, *Persicaria tinctoria* extract demonstrated pro-pigmenting activity through an ability to increase melanin production in skin explants and co-cultures of keratinocytes and melanocytes, albeit less prominently compared to the pro-pigmenting control. This nevertheless indicates its potential for enhancing tanning and UV protection by strengthening internal defences, facilitated by increased melanin production [15,16,17].

Additionally, treatment with *Persicaria tinctoria* extract led to enhanced mood and the release of β-endorphin and oxytocin in keratinocytes.

Interestingly, *Persicaria tinctoria* extract seems to act as a "molecular sun" by triggering the transcription of proopiomelanocortin (POMC), which is upstream of the melanin synthesis and well-being biological pathway through pro-peptide cleavage resulting in the release of α-MSH and β-endorphin [18,19,20].

The role of oxytocin in skin is not yet fully understood but it seems to be a promising molecule to soothe the skin and prevent skin ageing [12,21]. Moreover, a paper demonstrated a correlation between solar exposition and oxytocin level in skin [11]. The mode of action of *Persicaria tinctoria* extract in its activation is not fully understood: gene expression analysis showed significant increase (data not shown). However, this finding add a supplementary element to the hypothesis regarding the ability of *Persicaria tinctoria* extract to mimic the benefits of sunlight.

These findings position the extract's potential as a promising mood-enhancing ingredient in skincare formulations.

Moreover, the extract significantly stimulated vitamin D3 production in skin explants even without sun exposure. These biological effects are highly surprising and unprecedented in cosmetics. The extract may act as a precursor for vitamin D3 synthesis or may enhance the enzyme activity involved in this process. Further investigation to explore the underlying mechanism would be extremely valuable.

Nevertheless, results are promising, and suggests a potential to address vitamin D deficiency and support overall skin and body health, particularly in regions and seasons with limited sunlight [8,22,23].
Positive effects were observed *in vivo* in volunteers having applied the cream containing the extract. An overall low mood was improved with the decrease of tiredness and increase of affectionate mood, effects that can be linked to the modulation of β-endorphin, vitamin D and oxytocin, respectively, observed *in vitro* [5].

## Conclusion:

In summary, *Persicaria tinctoria* extract offers a multitude of benefits in skincare formulations including tanning activity, mood-enhancement and vitamin D3 stimulation. By mimicking the benefits of sunlight, including boosting well-being and enhancing skin health, incorporating *Persicaria tinctoria* extract into skincare products offers a promising avenue for addressing various skin concerns while also supporting holistic health.

### References:

[1] *G. L. Fell, K. C. Robinson, J. Mao, C. J. Woolf, and D. E. Fisher*, 'Skin β-Endorphin Mediates Addiction to UV Light', Cell, vol. 157, no. 7, pp. 1527–1534, Jun. 2014, doi: 10.1016/j.cell.2014.04.032.

[2] *N. T. Nguyen and D. E. Fisher*, 'MITF and UV responses in skin: From pigmentation to addiction', Pigment Cell Melanoma Res., vol. 32, no. 2, pp. 224–236, Mar. 2019, doi: 10.1111/pcmr.12726.

[3] *M. Brenner and V. J. Hearing*, 'The Protective Role of Melanin Against UV Damage in Human Skin †', Photochem. Photobiol., vol. 84, no. 3, pp. 539–549, May 2008, doi: 10.1111/j.1751-1097.2007.00226.x.

[4] *W. Z. Mostafa and R. A. Hegazy*, 'Vitamin D and the skin: Focus on a complex relationship: A review', J. Adv. Res., vol. 6, no. 6, pp. 793–804, Nov. 2015, doi: 10.1016/j.jare.2014.01.011.

[5] *A. Nowak et al.*, 'Effect of vitamin D3 on self-perceived fatigue: A double-blind randomized placebo-controlled trial', Medicine (Baltimore), vol. 95, no. 52, p. e5353, Dec. 2016, doi: 10.1097/MD.0000000000005353.

[6] *A. Religi et al.*, 'Estimation of exposure durations for vitamin D production and sunburn risk in Switzerland', J. Expo. Sci. Environ. Epidemiol., vol. 29, no. 6, pp. 742–752, Nov. 2019, doi: 10.1038/s41370-019-0137-2.

[7] *T. Koch*, '1831: the map that launched the idea of global health', Int. J. Epidemiol., vol. 43, no. 4, pp. 1014–1020, Aug. 2014, doi: 10.1093/ije/dyu099.

[8] *N. G. Jablonski and G. Chaplin*, 'Human skin pigmentation, migration and disease susceptibility', Philos. Trans. R. Soc. B Biol. Sci., vol. 367, no. 1590, pp. 785–792, Mar. 2012, doi: 10.1098/rstb.2011.0308.

[9] *T. T. Tran, J. Schulman, and D. E. Fisher*, 'UV and pigmentation: molecular mechanisms and social controversies', Pigment Cell Melanoma Res., vol. 21, no. 5, pp. 509–516, Oct. 2008, doi: 10.1111/j.1755-148X.2008.00498.x.

[10] *E. Culnan, J. D. Kloss, S. Darlow, and C. J. Heckman*, 'Associations between Seasonal Sleep Change and Indoor Tanning', Psychol. Rep., vol. 116, no. 2, pp. 523–533, Apr. 2015, doi: 10.2466/06.07.PR0.116k20w3.

[11] *N. Hayre*, 'Oxytocin Levels Inversely Correlate With Skin Age Score and Solar Damage', J. Drugs Dermatol., vol. 19, no. 12, pp. 1146–1148, Dec. 2020, doi: 10.36849/JDD.2020.5063.

[12] *V. Deing et al.*, 'Oxytocin modulates proliferation and stress responses of human skin cells: implications for atopic dermatitis', Exp. Dermatol., vol. 22, no. 6, pp. 399–405, Jun. 2013, doi: 10.1111/exd.12155.

[13] *T. Bechtold, A. Turcanu, S. Geissler, and E. Ganglberger*, 'Process balance and product quality in the production of natural indigo from Polygonum tinctorium Ait. applying low-technology methods', Bioresour. Technol., vol. 81, no. 3, pp. 171–177, Feb. 2002, doi: 10.1016/S0960-8524(01)00146-8.

[14] *L. G. Angelini, S. Tozzi, and N. Nassi o Di Nasso*, 'Environmental Factors Affecting Productivity, Indican Content, and Indigo Yield in Polygonum tinctorium Ait., a Subtropical Crop Grown under Temperate Conditions', J. Agric. Food Chem., vol. 52, no. 25, pp. 7541–7547, Dec. 2004, doi: 10.1021/jf040312b.

[15] *E. Kvam and R. M. Tyrrell*, 'The Role of Melanin in the Induction of Oxidative DNA Base Damage by Ultraviolet A Irradiation of DNA or Melanoma Cells', J. Invest. Dermatol., vol. 113, no. 2, pp. 209–213, Aug. 1999, doi: 10.1046/j.1523-1747.1999.00653.x.

[16] *B. Z. Zmudzka, V. J. Hearing, and J. Z. Beer*, 'Photobiologic role of melanin distribution in the epidermis', J. Photochem. Photobiol. B, vol. 84, no. 3, p. 231, Sep. 2006, doi: 10.1016/j.jphotobiol.2006.05.008.

[17] *M. J. Hoogduijn, E. Cemeli, K. Ross, D. Anderson, A. J. Thody, and J. M. Wood*, 'Melanin protects melanocytes and keratinocytes against H2O2-induced DNA strand breaks through its ability to bind Ca2+', Exp. Cell Res., vol. 294, no. 1, pp. 60–67, Mar. 2004, doi: 10.1016/j.yexcr.2003.11.007.

[18] *N. X. Cawley, Z. Li, and Y. P. Loh*, '60 YEARS OF POMC: Biosynthesis, trafficking, and secretion of pro-opiomelanocortin-derived peptides', J. Mol. Endocrinol., vol. 56, no. 4, pp. T77–T97, May 2016, doi: 10.1530/JME-15-0323.

[19] *R. Cui et al.*, 'Central Role of p53 in the Suntan Response and Pathologic Hyperpigmentation', Cell, vol. 128, no. 5, pp. 853–864, Mar. 2007, doi: 10.1016/j.cell.2006.12.045.

[20] *M. Oren and J. Bartek*, 'The Sunny Side of p53', Cell, vol. 128, no. 5, pp. 826–828, Mar. 2007, doi: 10.1016/j.cell.2007.02.027.

[21] *S. -Y. Cho, A. Y. Kim, J. Kim, D. -H. Choi, E. D. Son, and D. W. Shin*, 'Oxytocin alleviates cellular senescence through oxytocin receptor-mediated extracellular signal-regulated kinase/Nrf2 signalling', Br. J. Dermatol., vol. 181, no. 6, pp. 1216–1225, Dec. 2019, doi: 10.1111/bjd.17824.

[22] *A. Richard, S. Rohrmann, and K. Quack Lötscher*, 'Prevalence of Vitamin D Deficiency and Its Associations with Skin Color in Pregnant Women in the First Trimester in a Sample from Switzerland', Nutrients, vol. 9, no. 3, p. 260, Mar. 2017, doi: 10.3390/nu9030260.

[23] *S. S. Maeda et al.*, 'Seasonal variation in the serum 25-hydroxyvitamin D levels of young and elderly active and inactive adults in São Paulo, Brazil: The São PAulo Vitamin D Evaluation Study (SPADES)', Dermatoendocrinol., vol. 5, no. 1, pp. 211–217, Jan. 2013, doi: 10.4161/derm.24476.

**authors**

Morgane De Tollenaere, Anaïs Durduret, Emilie Chapuis, Jessy Martinez, Bénédicte Sennelier-Portet, Amandine Scandolera and Romain Reynaud

Givaudan Active Beauty

www.givaudan.com/active-beauty