Sustainable Cosmetic Innovation: Unlocking the Potential of Perilla Frutescens (Red Shiso) through Precision Indoor Farming

M-Letizia Campanari[1], Matthieu Kieny[1], Jeremy Espagnol[1], Severine Lasne[1], Estelle Loing[1]

[1]116 rue Louis Leprince Ringuet, 13013 , Næmos, Marseille, France

Sustainability in cosmetics requires ingredients that balance environmental, social, and economic factors. As these principles gain importance, research has increasingly focused on innovative solutions to meet them. This study integrates 'vertical' farming, which optimizes yield, resource efficiency, and spatial use while minimizing energy inputs, with “precision” farming, which customizes growing conditions to enhance the production of bioactive compounds. Eco-extraction method was also employed to improve efficiency, while avoiding the use of chemical solvent. Our approach was applied to *Perilla frutescens* (L.) Britton (Red Shiso) microgreens, a plant known for its edible and medicinal properties. Under indoor optimized conditions, the phytomolecular profile of Red Shiso microgreens showed a significant improvement compared to both the not-elicitated indoor condition and the Red Shiso available on the market. Finally, we assessed the potential of our extract for skin care applications. In UV-irradiated human skin models, treatment with 0.3% Red Shiso Microgreen extract enhanced epidermal barrier function and hydration by increasing

the expression of filaggrin, claudin, ceramides, and aquaporin 3 (AQP3). In conclusion, we have successfully developed a novel microgreen-derived extract from Red Shiso, enriched in targeted bioactive phytochemicals through controlled photostimulation. This next-generation cosmetic active exerts its photoprotective efficacy while embodies a sustainable and socially responsible innovation, addressing the growing demand for ethically formulated, science-driven dermocosmetic solutions.

1. Introduction

Sustainability has become a central focus in the cosmetics industry, driven by growing awareness among consumers and businesses about the environmental and social impacts of beauty products (1). Minimizing the environmental footprint of cosmetic ingredients while maintaining high-quality skin efficacy has become one of the industry's greatest challenges (2). This calls for innovative, natural, and eco-friendly ingredients (3) (4). Indoor farming has emerged as sustainable solution for integrating environmental considerations into the development of new skin actives without compromising performance (5). Indoor farming offers a sustainable solution by using less water and land, reducing chemical inputs, CO_2 emissions, and energy consumption (6). Furthermore, integration of “precision” in indoor farming allows for the cultivation of plants in a fully controlled indoor environment, regulating light, temperature, and humidity. This ecosystem offers full control

over every stage of active ingredient development and production, ensuring high levels of transparency and traceability—key advantages for the pharmaceutical and beauty industries. It also enables the integration of artificial intelligence (AI) and biotechnology to optimize plant growth and boost the production of bioactive molecules by precisely regulating environmental parameters—a concept known as Precise Indoor Farming (PIF) (7) (8) (9). *Perilla frutescens* (commonly known as Red Shiso) is a plant native from Asia with a long history of use in traditional medicine and culinary applications (10). It belongs to the Lamiaceae family, and there has been increasing interest in its potential applications in the cosmetic industry due to its beneficial antioxidant properties, which are attributed to its high content in phenolic compounds (10). In this study, we utilized PIF technology in conjunction with microwave-assisted extraction (MAE, (11)) to develop a novel Red Shiso microgreen extract, selectively enriched with targeted phytomolecules. This approach enabled us to precisely enhance the total phenolic compound (TPC) content, with a particular focus on rosmarinic acid (RA), caffeic acid (CA), and specific flavonoids that are highly relevant for cosmetic applications. Moreover, we highlighted the potential of this extract in modulating key epidermal barrier proteins—ceramides, filaggrin, claudin-1, and aquaporin 3 (AQP3)—which play a crucial role in maintaining skin integrity and hydration.

These proteins are often disrupted after UV exposure, further emphasizing the extract's relevance in skin health.

2. Materials and Methods

Plant material and culture: Perilla frutescens (L.) Britton (Red Shiso) seeds (Product ID:937) were purchased from Johnny's Seeds (955 Benton Ave, Winslow, ME 04901, US – MapQuest). The seeds were sown in a humid hemp matting substrate (350g/m²) in a growing room at a temperature of 25°C and 80% of humidity. They were kept in the dark, until germination. Then, the sprouts were transferred into another chamber where visible light was provided by LED system (Orius, LED4C3PR2) for 21 days (microgreen stage). Light spectrum, intensity and photoperiod are detailed in *table 1*. The microgreens were irrigated with a nutrient solution every day. Air temperature, relative humidity, and CO_2 concentration were set at 25°C, 70%, and 450 ppm, respectively. After harvesting, the microgreens were dried for 3 hours at 105°C, and dry weight (DW) was determined. A sample of fresh biomass and one of mature Red Shiso purchased from Shiso&Cie (Eyragues, France) were lyophilized, extracted with 60% ethanol and 40% water, and used for phytochemical analysis. The total phenolic content (TPC, expressed as mg GAE/g DW) was measured using the Folin–Ciocalteu method, and UPLC was used for the determination of polyphenols.

Table 1| Growth light parameters used in the experiments.

	Light spectrum	Total intensity (µmol.s.m²)	Photoperiod
Indoor Not-elicitated	1R/1B	300	12/12
Indoor Elicitated	2R/1B	300	24/0

Two different light spectrum composition (specifically the ratio of red light, ranging from 600 to 700 nm to blue light, ranging from 400 to 500 nm), luminous flux (light intensity) and daily light duration (photoperiod) were tested. µmol m^{-2} s^{-1} represents "micromoles per second per square meter".

Microwave-assisted extraction: Microwave-assisted extraction was carried out using a microwave extractor (Extractor E200, IDCO, Marseille, France). 1200g of frozen microgreens and 1200g of pre-heated (70°C) deionized water were mixed in the extraction vessel. A 1200W microwave power was applied for 15 minutes, followed by 15 minutes of agitation at 70°C. After extraction, the mixture was pressed to separate the liquid and solid fractions, then filtered using a plate filter.

Total phenolic content and polyphenols quantitation: The total phenolic content (TPC) was determined using the Folin-Ciocalteu reagent method. Absorbance was measured after 2 hours of dark incubation at 765 nm using a SpectroStar Nano spectrophotometer. The phenolic concentration was calculated by comparing the absorbance to a calibration curve of gallic acid solutions (100–1000 mg/L) and was expressed as gallic acid equivalents. Polyphenol quantification in the extracts was performed by using Ultra-High Performance Liquid Chromatography coupled with Mass Spectrometry (UPLC-MS), employing an Acquity UPLC Xevo-TQ system (Waters) and an Acquity BEH Shield RP18 column.

Reconstructed human epidermis model culture and explants culture: Reconstructed human epidermis (RHE) tissues from EPISKIN® (SkinEthic™ RHE/S/17), composed of Normal Human Epidermal Keratinocytes (NHEK), were used. Tissues were treated with Red Shiso extract at 0.3% and exposed to UV in cycles over several days. In total, tissues were treated for 24h and subjected to 12 min exposure at 4 J/cm^2 UVA and 374 mJ/cm^2 UVB. UV exposure was carried out in the UVACUBE 400 irradiation chamber (Dr Hönle AG). Skin explants from six Caucasian subjects were excised into 1 cm² fragments and cultured in inserts placed in wells, with the epidermis exposed to air. UVA (8 J/cm²) and UVB (0.5 J/cm²) radiations were applied on day 0 (D0) to induce skin oxidation. After UV exposure, Red Shiso extract was added to the culture medium at 0.3% daily for three days (D0, D1, D2). On day 3 (D3), skin fragments were fixed in formalin, embedded in paraffin, and analyzed immunohistochemically.

Staining and Image acquisition: RHE tissues were incubated with anti-ceramide (mouse, Sigma-Aldrich) and anti-AQP3 (rabbit, Sigma-Aldrich) antibodies. In explants, filaggrin (St John's Laboratory) was detected using a two-layer immunoperoxidase method (Impress kit, Vector Laboratories) and visualized with 3-amino-9-ethylcarbazole (AEC). Claudin 1 (clone PO4679, Eu) expression was assessed using a three-layer immunoperoxidase method (Polink-2 HRP kit,

Origene) and stained with AEC. All images were acquired with a Zeiss LSM 980 confocal microscope.

Statistical analysis: For HRE measurements, data were analyzed using GraphPad Prism V10.3.1. For *ex vivo* measurements, PRISM10 software was used.

3. Results

3.1. Effect of PIF on Red Shiso microgreen culture and bioactive compounds

Plants can sense and respond to light, affecting photosynthesis, morphology, and secondary metabolism (12). Red and blue lights are particularly important for promoting biomass and dry weight through photosynthesis (13) while longer light exposure can also accelerate crop growth (14). In this study, we examined the impact of spectral distribution and photoperiod on the phytochemistry of Red Shiso microgreens under constant light intensity. A red light (2R/1B) combination with a 24-hour light exposure elicited DW by 52% compared to a 1R/1B ratio and a 12/12-hour photoperiod (table 2). Caffeic acid, rosmarinic acid, apigenin-7-glucuronide, luteolin-7-glucuronide and TPC were also significantly increased by +62%, +307%, +203%, +110% and +79% respectively, with no significant change in flavonoid content (Table 2). Interestingly, the indoor elicitated microgreens were also superior to mature commercial Red Shiso, with increases in caffeic acid (+62%), apigenin-7-glucuronide (+400%), and luteolin-7-glucuronide (+84%).

Table 2| Biochemical responses of plants to growth light parameter.

	Yield Kg/m²	%DW	Cafeic acid g/kg (DW)	Rosmarinic acid g/kg (DW)	apigenin-7-glucuronide g/kg (DW)	lutéoline-7-glucuronide g/kg (DW)	TPC mg/ GAE g (DW)	TFC mg/ RUE g (DW)
Elicitated Red Shiso	1 kg/m²	12,27%	1,15	28,47	1,82	7,4	58,73	19,57
Not-elicitated Red Shiso	1 kg/m²	8,07%	0,71	7	0,6	3,53	32,83	20,95
Commercial Red Shiso	-	-	0,71	32,67	0,36	4,03	58,17	18,6

A comparative analysis demonstrating the beneficial effects of a 24-hour photoperiod (continuous light without a night phase) and an enhanced red-light spectrum on dry biomass production and phytochemical composition, compared to light conditions mimicking the native environment of Red Shiso and commercially available mature Red Shiso. TPC, total phenolic compounds; TFC, total flavonoid compounds.

3.2. Red Shiso microgreens extract increases skin barrier strength and hydration

UV radiation is a major cause of skin aging, leading to oxidative damage and disrupting molecules crucial for the epidermal barrier and hydration. It negatively impacts ceramides (15), important for the stratum corneum, and Claudin 1 (16), a protein in tight junctions. UV exposure also reduces aquaporin 3 (AQP3) (17) and filaggrin (18), both essential for skin hydration. In both RHE and *ex vivo* models, 0.3% of Red Shiso microgreens extract resulted in a significant increase in ceramides (+44.6%, figure 1 A), claudin 1 (+153%, figure 1 B), AQP3 (+17.6%, figure 1 C), and filaggrin (+139%, figure 1 D) levels compared to control conditions exposed to UVs.

4. **Conclusion**

In conclusion, our study demonstrates that treatment with 0.3% Red Shiso microgreen extract developed by PIF technology, significantly enhances the skin's barrier function, as evidenced by the increase in ceramides, filaggrin, claudin 1 and AQP3 expression, compared to untreated UV-exposed skin models. These findings suggest that Red Shiso microgreen extract plays a crucial role in supporting skin barrier integrity and hydration, making it a promising candidate for mitigating

UV-induced photodamage. Additionally, our study highlights the potential of integrating sustainable farming practices in the cosmetic industry, specifically using precision indoor farming techniques. This approach not only maximizes product efficacy but also promotes environmental sustainability, offering a novel and responsible strategy for future skincare solutions.

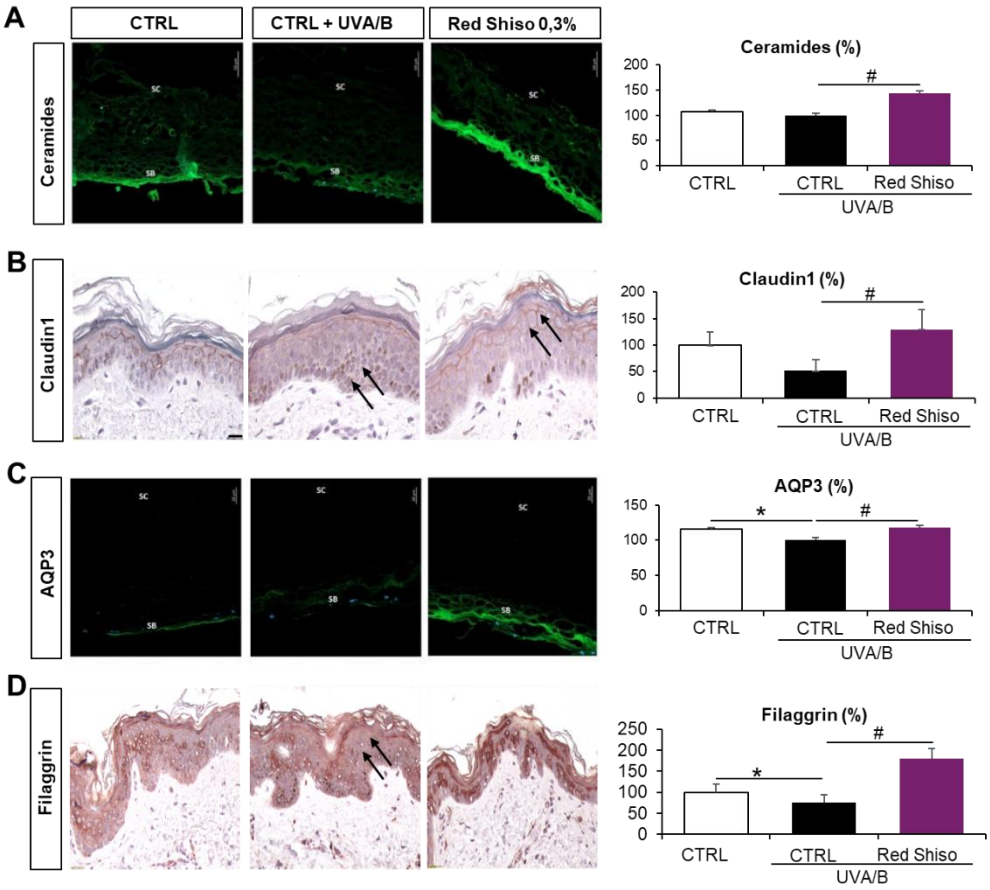

Figure 1 | A) Effect of Red Shiso Microgreen extract on ceramides synthesis. Left, ceramides immunolabelling in RHE. Scale bar: 50 µm. Right, Bar graph showing ceramide quantification. One-way ANOVA test followed by Dunnett's post hoc multiple comparisons test. (#) CTRL + UVs vs Shiso extrait at 0,3% + UVs (n= 12, p=0,0001). **B) Effect of Red Shiso extract on Claudin1 synthesis.** Left, Claudin1 immunolabelling in explants. X400, scale bar: 20 µm. Right, Claudine1 quantification. t-test. (#) CTRL + UVs vs Shiso extrait at 0,3% + UVs (n= 6, p=0,0045). **C) Effect of Red Shiso extract on AQP3 synthesis.** Left, AQP3 immunolabelling in RHE. Scale bar: 20 µm. Right, AQP3 quantification. (*) CTRL vs CTRL + UVs (n= 12, p=0,0216). (#) CTRL + UVs vs Shiso extrait at 0,3% + UVs (n= 12, p=0,0058). **D) Effect of Red Shiso extract on Filaggrin synthesis.** left, Filaggrin immunolabelling in explants. X200, scale bar: 50 µm. Right, bar graph showing Filaggrin quantification. t-test. (*) CTRL vs CTRL + UVs (n= 6, p=0,049). (#) CTRL + UVs vs Shiso extrait at 0,3% + UVs (n= 6, p=0,005). SC: stratum corneum; SB: stratum basale.

1. Singh, Aditya & Singh, Vishal. (2022). **Sustainable ecosystem in cosmetic industries**. Thesis.
2. Vanaria RJ, *et al.* (2025). **Environmental Impact and Sustainability Associated with the Practice of Dermatology**. J Clin Aesthet Dermatol. 40078861, 18(2):50-55.
3. Dini I, Laneri S. (2021). **The New Challenge of Green Cosmetics: Natural Food Ingredients for Cosmetic Formulations.** Molecules. 26, 34206931, 26(13):3921.
4. Martins AM and Marto JM. (2023). **A sustainable life cycle for cosmetics: From design and development to post-use phase, Sustainable Chemistry and Pharmacy**. 35, 101178, ISSN 2352-5541.
5. Ampim PAY, Obeng E, Olvera-Gonzalez E. (2022). **Indoor Vegetable Production: An Alternative Approach to Increasing Cultivation.** Plants (Basel).11(21):2843.
6. Abdelfatah, Mohab & El-Arnaouty, Sahar. (2023). **A review of vertical farming for sustainable urban food security.** 6. 214-231.
7. Marondedze C, *et al.* (2018). **Towards a tailored indoor horticulture: a functional genomics guided phenotypic approach.** Hortic Res. 30393542, 5:68.
8. Li CX, *et al.* (2017). **An RNA-Seq Analysis of Grape Plantlets Grown in vitro Reveals Different Responses to Blue, Green, Red LED Light, and White Fluorescent Light**. Front Plant Sci. 10., 8:78.
9. Teo, Z.W.N., Yu, H. (2024). **Genetic breeding for indoor vertical farming**. npj Sustain. Agric. 2, 13.
10. Wu X *et al.* (2023). **Perilla frutescens: A traditional medicine and food homologous plant.** Chin Herb Med. 15(3):369-375.
11. Bagade SB, Patil M. (2021). **Recent Advances in Microwave Assisted Extraction of Bioactive Compounds from Complex Herbal Samples: A Review.** Crit Rev Anal Chem. 51(2):138-149.
12. Dou, Haijie & Niu, Genhua & gu, Mengmeng. (2019). **Photosynthesis, Morphology, Yield, and Phytochemical Accumulation in Basil Plants Influenced by Substituting Green Light for Partial Red and/or Blue Light**. HortScience. 54. 1769-1776.
13. Meng, Qingwu & Runkle, Erik. (2019). **Far-red radiation interacts with relative and absolute blue and red photon flux densities to regulate growth, morphology, and pigmentation of lettuce and basil seedlings.** Scientia Horticulturae. 255. 269-280.
14. Warner, R.; Wu, B.-S.; MacPherson, S.; Lefsrud, M. (2023). **How the Distribution of Photon Delivery Impacts Crops in Indoor Plant Environments: A Review**. Sustainability. 15, 4645.
15. Takagi Y, *et al.* (2004). **Decreased levels of covalently bound ceramide are associated with ultraviolet B-induced perturbation of the skin barrier**. J Invest Dermatol. 123(6):1102-9.
16. Takuo Y et al. (2011). **Characterization of Tight Junctions and Their Disruption by UVB in Human Epidermis and Cultured Keratinocytes.** Journal of Investigative Dermatology, Volume 131, Issue 3, 744 – 752.
17. Tang SC, *et al.* (2019). **Glycolic acid attenuates UVB-induced aquaporin-3, matrix metalloproteinase-9 expression, and collagen degradation in keratinocytes and mouse skin.** Biochem J. 476(10):1387-1400.
18. Scott IR. (1986). **Alterations in the metabolism of filaggrin in the skin after chemical- and ultraviolet-induced erythema**. J Invest Dermatol. 87(4):460-5.