Damaged skin: New Data on *Centella asiatica* for an Accelerated Skin Integrity Recovering

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Introduction

***Centella asiatica* extract** (CAE, INCI: Asiaticoside - Madecassic Acid - Asiatic Acid) is a leaves extract of the Malagasy plant, which has been selected for its high stable composition in pentacyclic triterpenes. These molecules participate in the natural defences of the plant and are known for their dermo-cosmetic benefits [1].

Normal wound repair is a dynamic and complex process involving multiple coordinated interactions between various skin cells and signalling molecules [2]. Three main phases, which are inflammation, reconstruction and remodeling, ultimately lead to tissue regeneration [3]. But any failure during the repair process may cause chronic wounds or scar formation.

The benefits of CAE on skin repair process were evaluated *in vitro*, through the testing of its components alone or in combination, on the regulation of inflammation and cellular protection on keratinocytes. Then, the reconstruction process was studied on dermal cells regarding migration and cell protection. The remodeling phase was addressed through the contraction and protection of the neo synthesized extracellular matrix (ECM), and the regulation of the vascular network.

Finally, a clinical study was conducted to evaluate the repairing effect of CAE on damaged skin.

Materials & Methods

❶ BIOLOGICAL EVALUATION

➲ **Soothing properties via IL-1α release and antioxidant efficacy were studied in keratinocytes** (NHEK and HaCaT respectively). Cells were treated for 24h with CAE, exposed to UVB and treated again for 24h. IL-1α was quantified by ELISA and intercellular oxidation level using DCFH-DA test.

➲ **Reconstruction benefits of CAE were evaluated on fibroblasts** (NHDF) migration by fluorescence and anti-glycation properties by detection of DNA fragmentation by ELISA.

➲ **Remodeling properties were assessed on ECM protection and vascular network regulation**. NHDF were treated with CAE and differentiation was evaluated by measuring α-SMA (α-Smooth Muscle Actin, western blot).
Fibers' contraction by fibroblasts was studied in a 3D model treated with CAE. And, a co-culture of keratinocytes and fibroblasts was treated for 48h with CAE to study after induction by TNF-α, MMP-1 and MMP-9 release (quantified by ELISA). Vascular network maturation was evaluated by measuring the quantity of VEGF and TSP-1 (ELISA), in NHEK/NHDF co-culture and HUVEC cells respectively, after a 48h treatment with CAE and induction by TGF-β [4].

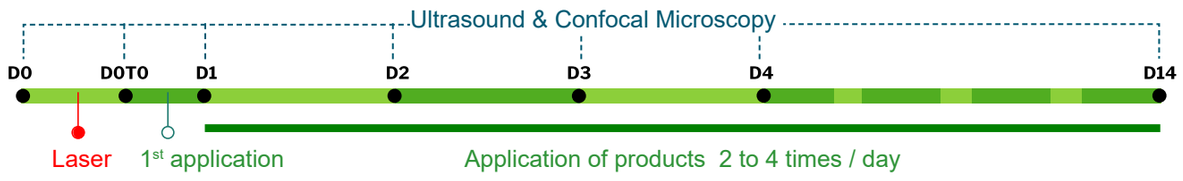
❷ CLINICAL STUDY

A randomized double blind placebo controlled study was conducted to evaluate the effects of a formula containing 0.2% of CAE on damaged skin.

> *20 women from 24 to 61 years-old planning to have a laser intervention were recruited. Respecting the integrity of the epidermis, a non-ablative fractional laser created thermal lesions within the dermis, defined as micro-thermal zones (MTZ), generating both inflammation and ECM damages inducing the repair process. The laser also induced an inflammation within the epidermis.*

The repairing effect of CAE was evaluated at different time points from D0 to D14 using:

- Confocal Microscopy by reflectance (Vivascope® 3000) that allows visualization of the epidermis [5].
- High Resolution Ultrasound (50 MHz) (DUB®SkinScanner75) to analyze the dermis structure [6].



References:

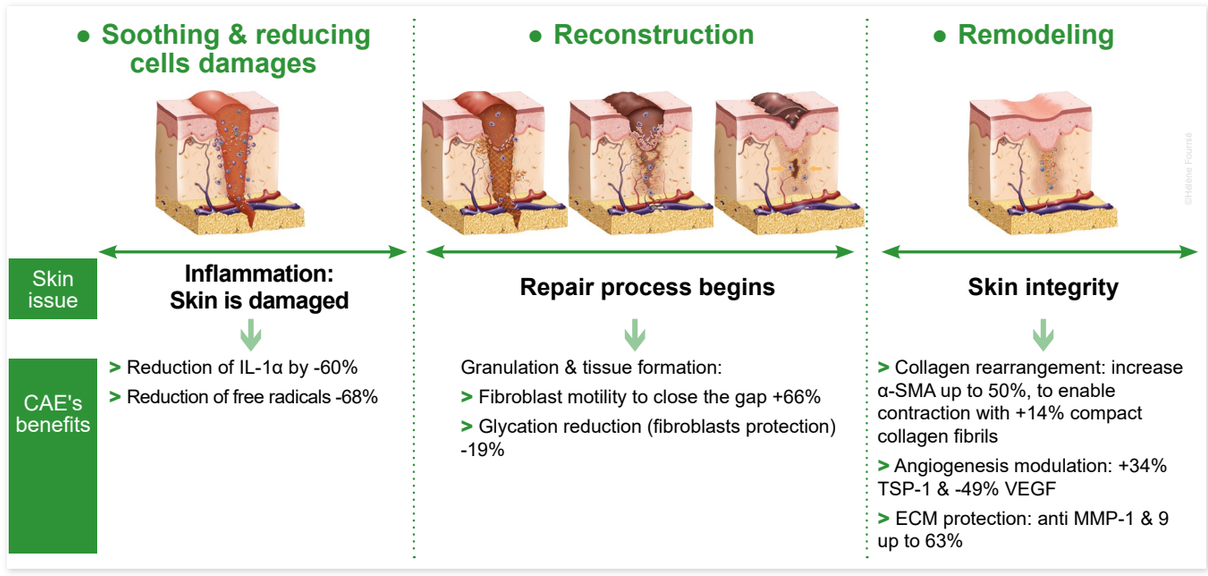
1. Segond C, Lepetit JC, Petit V, Theron E, Loiseau A (2005). *Latest results on Centella asiatica from wound healing mechanism to cosmetic uses*. New York Society of Cosmetics Chemists, USA.
2. Su L, Zheng J, Wang Y, Zhang W, Hu D (2019). *Emerging progress on the mechanism and technology in wound repair*. Biomedicine & Pharmacotherapy. 117:109191.
3. Hinz B, Pittet P, Smith-Clerc J, Chaponnier C, Meister JJ (2004). *Myofibroblast development is characterized by specific cell-cell adherens junctions*. Mol Biol Cell. 15(9):4310-20.
4. Nakagawa T, Li JH, Garcia G, Mu W, Piek E, Böttinger EP, Chen Y, Zhu HJ, Kang DH, Schreiner GF, Lan HY, Johnson RJ (2004). *TGF-beta induces proangiogenic and antiangiogenic factors via parallel but distinct Smad pathways*. Kidney Int. 66(2):605-13.
5. Levine A, Markowitz O (2018). *Introduction to reflectance confocal microscopy and its use in clinical practice*. JAAD Case Rep. 4(10):1014-1023.
6. Polańska A, Dańczak-Pazdrowska A, Jałowska M, Żaba R, Adamski Z (2017). *Current applications of high-frequency ultrasonography in dermatology*. Postepy Dermatol Alergol. 34(6):535-542.
7. Mallol J, Belda MA, Costa D, Noval A, Sola M (1991). *Prophylaxis of Striae gravidarum with a topical formulation. A double blind trial*. Int J Cosmet Sci. 13(1):51-7.
8. Laugel C, Cohen-Letessier A, Clement A, Laverdet C, Legmann P, Marty J.P (1999). *Evaluation of the clinical and echographic efficacy of a cream with Centella asiatica in the treatment of stretch marks.* Les Nouvelles dermatologiques.18:412-16.

Conclusion

This research helped to objectify the benefits of CAE on the skin repair process. It enabled highlighting a very complete mode of action both *in vitro* and *in vivo*. This work allowed to demonstrate the efficacy of CAE to boost skin regeneration after a dermatological intervention.

Results & Discussions

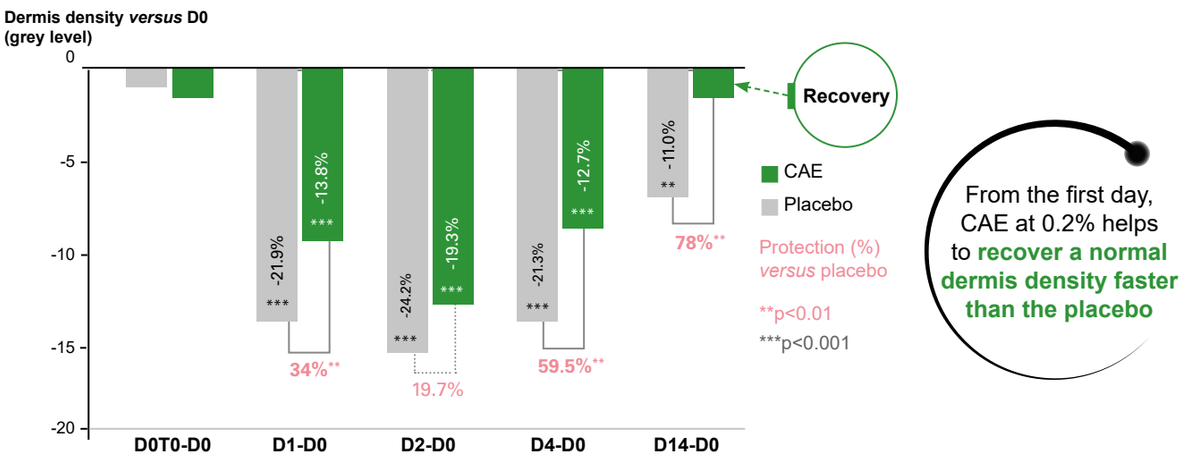
❶ BIOLOGICAL EVALUATION



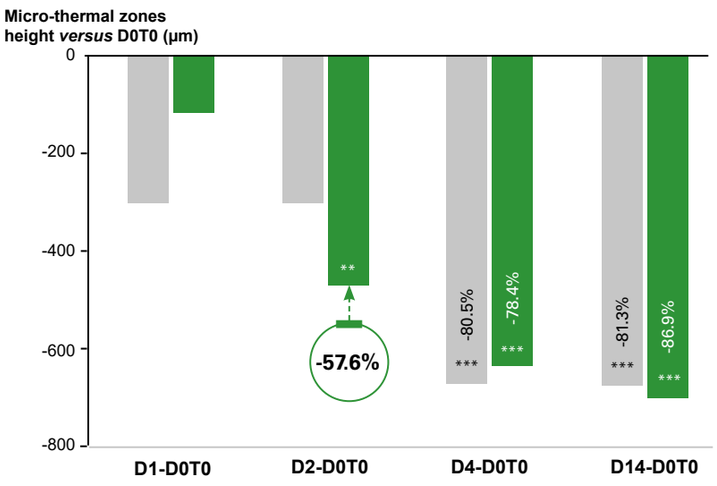
❷ CLINICAL STUDY

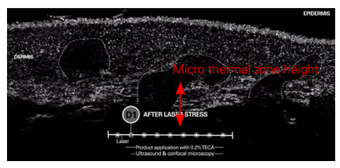
Evaluation of the dermis density *versus* D0 by High Frequency Ultrasound Microscopy

A decrease in the dermis density reveals an alteration of the tissues and an increase of the inflammation



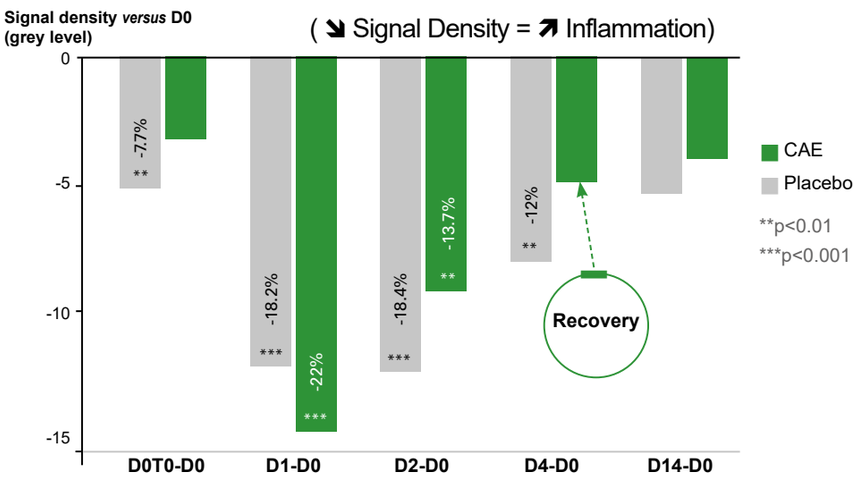
Evaluation of the micro-thermal zones height by High Frequency Ultrasound Microscopy **in the dermis *versus* D0T0**





From 2 days, CAE at 0.2% **reduces by -57.6% the lesions' height**

Evaluation of the inflammation in the epidermis by Confocal Microscopy ***versus* D0**



After 4 days, CAE at 0.2% **resolves the inflammation** 10 days before placebo

Discussion The *in vitro* data indicated that CAE had a strong efficacy on the three steps of the skin repair process as its components were able to induce a soothing and protective effect on epidermal cells, to improve tissue reconstruction and remodeling.

These benefits were confirmed in a clinical trial, in which CAE helped for a faster dermal density recovery, reduction of the lesions and resolution of the inflammation in comparison with placebo after laser intervention. Thus, CAE was able to accelerate the skin repair process and the reduction of the inflammation. These observations are in accordance with the scientific literature demonstrating the preventive and curative effects of CAE on skin repair process on stretch-marks [7,8].