

Boira, Clodé¹; Meunier, Marie¹; Scandola, Amandine¹; Bracq Marine¹; Sandré Jérôme²; Maramaldi, Giada¹; Reynaud, Romain¹
¹Givaudan Active Beauty, France; ²Polyclinique Courlancy, France

Introduction:

Several biological mechanisms are affected by the natural ageing of the body, the large majority of them starting from a modification of gene control and ending up in visible skin ageing signs [1]. Pluripotent stem cells present an amazing vitality and can turn into different tissues to replace senescent cells, but their proliferation capacity starts decreasing throughout the natural ageing of cells [2]. As they age, stem cells progressively lose their DNA repair capacities, their ability to produce new progenitors and differentiated effector cells is impacted [3]. Tissue regenerative potential reduces, associated to an accumulation of non-functional cells throughout life [4].

Stem cells present an important role in different skin layers. The epidermis is the first part of the body to be exposed to external aggressors and needs a constant renewal due to its high turnover [5]. Stem cells are also present into the dermal tissue and participate in the homeostasis maintenance and regeneration of injured skin [6]. By losing their pluripotency and functionality, skin cells show a slowing down of cells regeneration and repair function leading to a progressive apparition of visible ageing signs such as wrinkles or eye-bags [7].

We hypothesized that reactivating cell memory to bring them back closer to a pluripotency state would be a very effective and innovative strategy for cells rejuvenation.

In Tanzania, a very typical plant of the miombo forest environment is *Terminalia sericea*, a beautiful, majestic tree with silvery leaves, also known as a silver tree. In the bark of the roots of this tree, the plant accumulates a specific pentacyclic terpenoid: Sericoside. Sericoside is already known and largely used for its medicinal properties [8].

In this study, we evaluated the capacities of Sericoside to reprogram cells to a younger stage to define if it could be an efficient candidate to reactivate cell memory for a rejuvenation process.

Materials & Methods:

In vitro studies

Transcriptomic study	Cell proliferation
- Normal Human Dermal Fibroblasts (NHDFs)	- NHDFs
- Sericoside 0.02% for 24h	- Senescence chemically induced with H2O2
- RT-qPCR with specific plates designed to study cell rejuvenation	- Sericoside 0.02% for 72h
	- Comparison with untreated senescent NHDFs and with untreated young NHDFs (22 yo)

Clinical evaluation

Panel description	Skin texture and roughness
- Placebo controlled single blind clinical study	- DermaTOP-Blue method: skin profilometry
- 40 volunteers - 2 groups (aged 35-55)	- Rz average & Ra maximum = 3D skin roughness
- Twice daily application of an emulsion containing 0.5% Sericoside versus placebo over 1 month.	- Sa parameter = skin texture.
Skin firmness and fatigue	Eye contour benefit
- Cutometer® MPA 580	- Chromameter®
- R2 parameter = skin firmness	- L parameter = 0=black; 100=white
- R9 parameter = skin fatigue	- a parameter = green-red
	- b parameter = blue-yellow

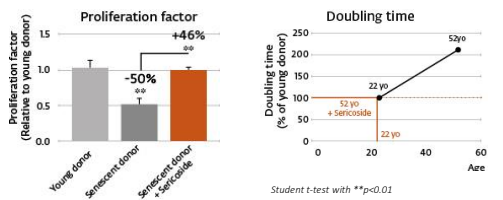
Results & Discussion:

1. Genes modulation and cell reprogramming

DNA repair	GADD45A +29%* ; OGG1 +56%** ; XPA +26%*** ; XPC +51%*
Pluripotency TF	NANOG +36%* ; POU5F1 +51%*
RA receptor	CRABP2 +47%*
Signal transduction	CAV1 +286%**
Stem cell maintenance	SOX2 +200%#
Transcription factor	MYC +39%*

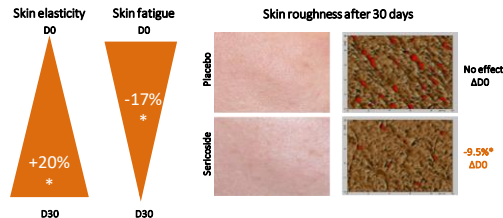
Student t-test with #p<0.1 ; *p<0.05 ; **p<0.01 ; ***p<0.001

2. Improvement of senescent cells proliferation



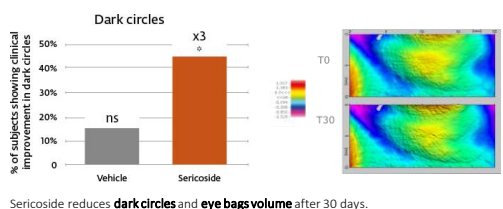
Sericoside: **2-times increased senescent cells' proliferation.**
Rejuvenation of cells presenting a **doubling time** equivalent to a **22 years old donor.**

3. Reversing the clock of age



Sericoside **increased skin elasticity** and **decreased skin fatigue** after 30 days. It also improved skin texture by decreasing skin roughness after 30 days.

4. Eye contour benefit



Conclusions:

Thanks to this study, we proved that reprogramming cells by stimulating the natural tools available in our DNA is an innovative way to rejuvenate the skin. Sericoside proved its strong efficacy on this innovative strategy.

Acknowledgements:

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