

Redensyl®

Reactivates hair follicle stem cells for an astonishing hair growth

The scalp bears an average 110,000 hair follicles which are growing and falling on a daily basis. When the balance between the growing hair and the falling ones is altered, then hair loss starts and baldness appears.

To reverse this phenomenon referred to as alopecia, Redensyl® dramatically reactivates hair growth and decreases hair loss with clinically visible results in 3 months by:

- 1) Re-launching stem cells activity and proliferation
 - › The outer root sheath stem cells (ORSc) are vitalized, thus triggering a new hair cycle;
- 2) Increasing the dermal papilla's fibroblasts metabolism
 - › Hair follicles are nourished resulting in the stem cells switching on the anagen phase faster.

Hair Growth Galvanizer

Focus on the product

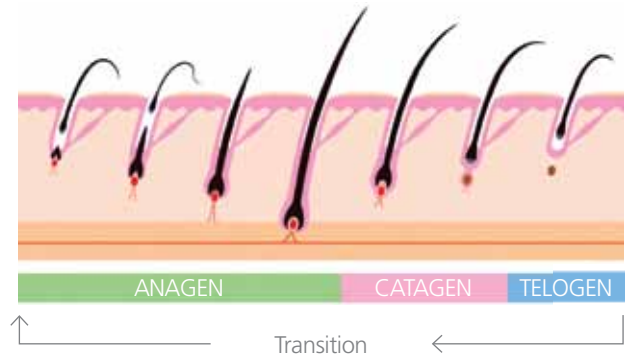
Hair loss in numbers

It is a known fact that 40% of men will have noticeable hair loss (alopecia) by age 35. This number reaches 65% by 60 years of age. Women are also deeply impacted by such process: 50 to 75% suffer noticeable hair loss by age 65. Hair loss can be devastating to one's self image and emotional well being.

The normal cycle for hair

The hair cycle is made of three phases:

- Anagen phase during which the hair is growing (\pm 3 years),
- Catagen phase also called the transition phase (\pm 3 weeks),
- Telogen phase during which the hair is dying and falling (\pm 3 months), which is followed by the anagen phase again.



Hair loss and stem cells

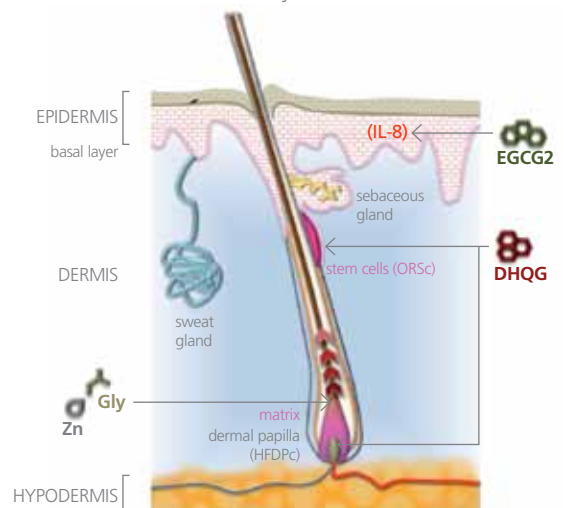
When suffering from hair loss, the telogen phase is prolonged, and the transition to the anagen phase becomes more difficult. Hair become thinner and the percentage of hair transitioning to the telogen phase continues to increase.

The problem comes from the fact that the hair follicle stem cells (also called ORSc) located in the bulge along the hair, are less productive, and less adapted to improve the quality of the matrix (made of keratinocytes) supporting the hair follicle growth. Furthermore, the fibroblasts located in the dermal papilla (also called HFDPc) are less efficient in communicating with the stem cells, meaning that the matrix will not be renewed as it used to. Initiating the anagen phase becomes more sluggish, and hair loss becomes a part of daily life.

Redensyl[®]: acting on stem cells and HFDPc to re-activate hair growth

Redensyl[®] is made of patented molecules targeting the ORSc and the HFDPc at the same time for a better efficiency:

- Dihydroquercetin-glucoside (DHQG): a stabilized polyphenol which activates the division of hair follicle stem cells, while maintaining their differentiation properties. It protects stem cells from apoptosis (BCL2 activation), and drives them towards the anagen cycle (β -catenin activation), while boosting the metabolism of dermal papilla fibroblasts.
- EGCG-glucoside (EGCG2): a stabilized EGCG derivative used to reduce the typical inflammatory state of alopecic scalp (reduction of IL-8), and capture free radicals¹.
- Glycine: a major constituent of hair proteins, mainly keratin associated proteins (KAP), which favors hair growth².
- Zinc: a very important co-factor for numerous enzymes, favoring the incorporation of cystin in keratin for a stronger hair shaft³.



Redensyl[®] shows outstanding results after 3 months at the clinical level.

1. Source: Chem Phys Lipids. 2000 Jun ; 106(1):53-63.

2. Source: J Invest Dermatol. 1994 Sep;103(3):310-7.

3. Source: J Nutr. 1971 Apr;101(4):445-52.

Biological activity

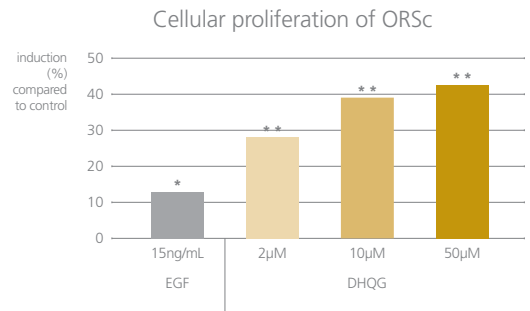
Four actions on ORSc stem cells (*in vitro* tests)

1. Stimulating ORSc proliferation:

ORSc proliferation was tested with increasing concentration of dihydroquercetin-glucoside (DHQG, the major component of Redensyl®) by following the BrdU cell proliferation assay, using EGF as a reference. Measurement of cell proliferation is proportional to the amount of incorporated BrdU.

Results: DHQG increases the cellular proliferation of the ORSc. More stem cells are produced with increasing doses of DHQG.

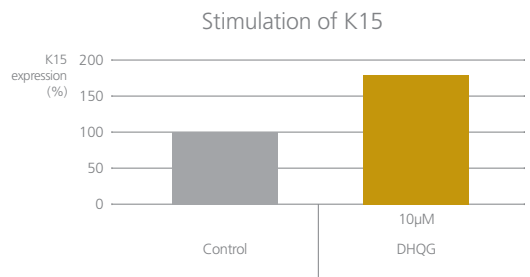
* $p < 0.01$, ** $p < 0.001$ compared to control, Student's t-test



2. Maintaining their stem cell's phenotype:

ORSc were treated with 10µM of DHQG to evaluate the potential of this molecule to maintain the ORSc as real stem cells. The mRNA expression of cytokeratin 15, a major stem cell marker, was quantified by qRT-PCR.

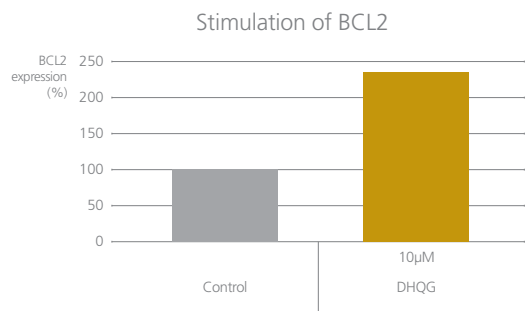
Result: DHQG at 10µM multiplies by almost 2 times the mRNA synthesis of K15, a qualification marker of stem cell's phenotype.



3. Avoiding apoptosis:

ORSc were treated with 10µM of DHQG to evaluate the protective potential of this molecule against apoptosis. The mRNA expression of BCL2, a major anti-apoptotic marker, was evaluated by qRT-PCR

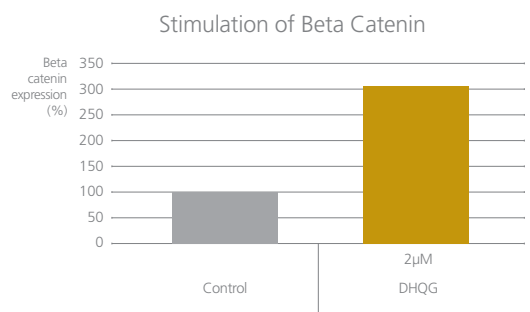
Result: DHQG at 10µM increases by 2 times the mRNA synthesis of BCL2, showing the anti-apoptosis effect of this molecule.



4. Activating differentiation:

ORSc were treated with 2µM of DHQG to evaluate the potential of this molecule to induce the cells differentiation process. The mRNA expression of β-catenin, a major differentiation marker, was quantified by qRT-PCR.

Result: DHQG at 2µM multiplies by more than 3 times the mRNA synthesis of β-catenin, showing its differentiation inducing activity on stem cells.



Summary: DHQG stimulates hair follicle stem cells division, maintains their stem cells status, protects them from apoptosis, and boosts their differentiation.

Biological activity

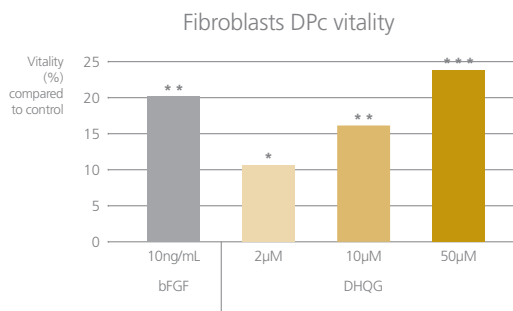
Increase of Fibroblasts DPc vitality (*in vitro* tests)

Human fibroblasts dermal papilla cells (HFDPC) were incubated for 48 hours in a basal medium and treated with increasing doses of DHQG (the major component of Redensyl®) or bFGF as a reference.

Their metabolic activity was evaluated thanks to a XTT reduction assay.

Results: DHQG helps the HFDPC to improve their metabolic activity, for a better nourishment of the hair follicle.

*p<0.05, **p<0.01, ***p<0.001 compared to control, Student's t-test

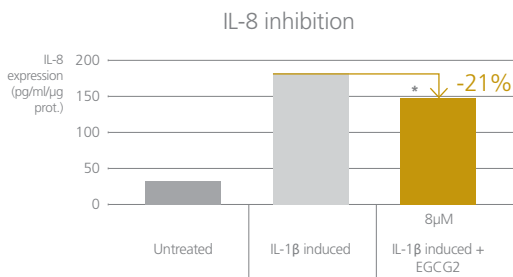


Decrease of skin irritation (*in vitro* tests)

EGCG2 was tested for its ability to reduce IL-8, a cytokine involved in scalp irritation. An irritated skin is more prone to hair loss. Normal human keratinocytes were put in a culture medium and were stressed using IL-1β and treated for 48h with EGCG2, a major component of Redensyl®. IL-8 in the supernatant was quantified by ELISA test.

Results: EGCG2 confirms its anti-irritation potential by inhibiting IL-8 release by 21%.

*p<0.05 compared to untreated, Student's t-test



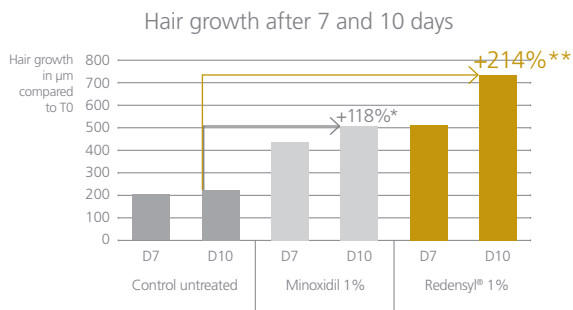
Increase of hair follicle length (*ex vivo* Philpott test)

Redensyl® was tested at 1% versus Minoxidil at 1% as a benchmark reference to evaluate its potential on hair follicle growth. Hair of four male donors suffering from alopecia were maintained alive in normal hair culture conditions. After 7 and 10 days hair growth was measured compared to day 0 with pictures analysis.

Results: Redensyl® increases hair growth by +214% compared to untreated, and shows almost two times higher results than Minoxidil, the benchmark reference.

*p<0.1, **p<0.001 compared to untreated, Student's t-test

Visible increase of hair follicle size



Efficacy

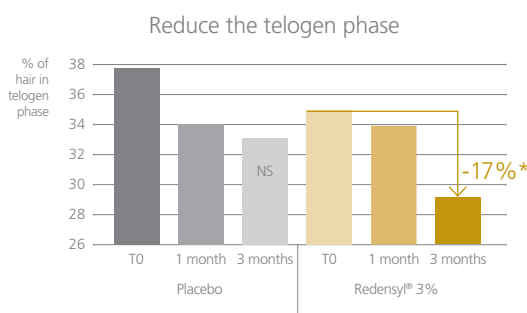
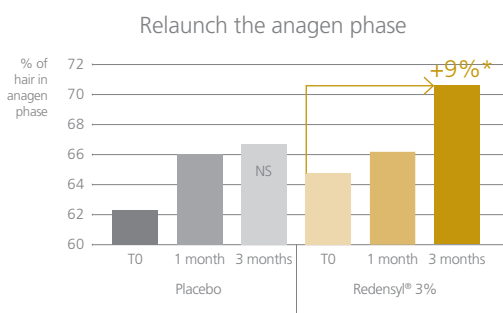
Reactivate the hair growth cycle (clinical evaluation)

The efficiency of Redensyl® at 3% was evaluated in a double-blind test versus a placebo. Twenty six male volunteers were selected by following specific inclusion criteria: between 18 to 70 years old, brown to dark hair, with a minimum density of hair of 150 hair/cm² and 40 telogen hair/cm², with clinically confirmed grade 3 to 4 alopecia.

Volunteers applied the placebo or the product with 3% of Redensyl® on their whole scalp daily for 3 months.

A shaved area of 1.5cm² was defined on each volunteer to allow the measurements on a window of 0.7cm² at D0, D28 and D84.

Phototrichograms were realized using a NIKON camera associated with Canfield® Epiflash System and a contact plate to press hair on the scalp. Analysis were run with Photoshop CS5 extended® and permitted to define if hair were in anagen, telogen or undetermined phase.



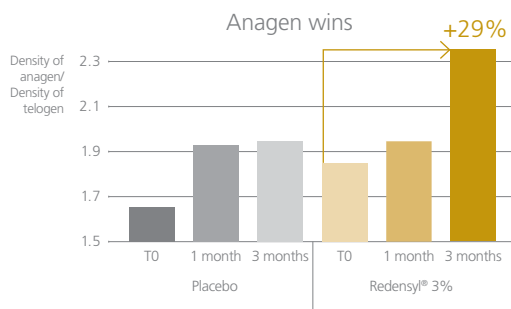
*p<0.01 compared to untreated, Student's t-test

Results: A non significant placebo effect is observed (mechanical activation of micro-circulation), with almost no more evolution after 1 month. Redensyl® increases the percentage of hair in anagen phase by 9% compared to T0 after 3 months, and decreases the percentage of hair in the telogen phase by 17% compared to T0 after 3 months.

Rebalance the anagen/telogen ratio (clinical evaluation)

The ratio Anagen/Telogen was evaluated by comparing the density of hair in anagen phase and in telogen phase.

Results: Redensyl® significantly increases the ratio Density of Anagen / Density of Telogen. After 3 months the ratio reaches 2.37 while the placebo shows almost no evolution after one month.



As a consequence, density of hair was also measured and was increased by an average +8% in three months while using Redensyl® at 3%.

Efficacy

Redensyl®: Visible results after 3 months (clinical evaluation)

85% of volunteers show clinical improvements. More anagen hair, a higher density, more visible hair.

Examples of the clinical results of three volunteers (29 to 52 years old) treated with Redensyl® during 3 months.

Criteria	Volunteer	#3 (52 years old)	#6 (42 years old)	#26 (29 years old)
% of new anagen hair		+ 10.8%	+ 19.2%	+ 9.2%
% of density of hair increase		+ 17%	+ 17%	+ 17%
Number of new hair / cm ²		+ 47 hair/cm ²	+ 43 hair/cm ²	+ 29 hair/cm ²
Total number of new hair on their scalp (600 cm ²)		+ 28,200 hair	+ 25,800 hair	+ 17,400 hair
Number of new hair per month on their scalp		+ 9,400 hair	+ 8,600 hair	+ 5,800 hair

Macro pictures (Phototrichograms)

Results: Hair look thicker, with a visible improvement of the density.

J0



3 months



J0



3 months



J0



3 months



Scalp pictures

Results: Hair loss stopped, a visible increase of hair density is noticeable.

Before



After



Before



After



Before



After

