CRESCINA®

RE-GROWTH

HFSC

TRANSDERMIC TECHNOLOGY

It Helps Promote the Physiological Hair Growth. 100% Formula

Effective in 100% of the subjects tested

8 PATENTS: SWITZERLAND AND EUROPE

TECHNICAL MANUAL

LABO

LABO COSPROPHAR

Crescina Transdermic HFSC

Swiss and European Patents

SWISS PATENT CH 703 390

SWISS PATENT CH 711 466

SWISS PATENT CH 697 229

SWISS PATENT CH 693 815

SWISS PATENT CH 693 814

SWISS PATENT CH 693 816

SWISS PATENT CH 704 629

EU PATENT EP 2 561 858

SWISS
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1. Introduction

The Company

"Labo" identifies two realities:

- The **Swiss company**, based in Basel (Switzerland), named Labo Cosprophar AG, which is responsible for research and development activities. Labo Cosprophar holds most of the industrial and intellectual property of Labo's products (incorporated in 1986);

- The **Italian company**, based in Padua (Italy), named Labo International srl, focuses its activities on strategic and operational marketing for Italy and the rest of the world. Labo International holds the licenses for production and distribution of products (incorporated in 1996).

Their mission is to make relevant investments in research, design and production of value-added cosmetic products.

After products' tests in the Italian market, distribution is extended at global level.

International Distribution

Today Labo distributes Crescina, Fillerina and Labo Transdermic across 33 Countries, but between 2019 and 2022, 38 new Countries are expected to be covered.

Photographic reproduction of the Scale of male thinning, according to Hamilton / Norwood classification.

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Crescina Re-Growth: the Milestones

Crescina Re-Growth has always focused on hair thinning. It has been formulated to help prevent and treat hair thinning dependent on physiological not pathological causes and when the quality and quantity of hair gradually decreases due to a disrupted activity of the hair follicles.

Crescina is a treatment in vials: the formulae (specific for man and woman) are continuously improved to make them more and more effective. The study on the progression of hair thinning, classified by international experts and codified by the Scale of Hamilton / Norwood (male thinning) and by the Scale of Ludwig / Savin (female thinning), allowed to develop formulations with diversified concentrations of active ingredients suitable to treat the different stages of the problem.

Crescina was first produced in 1998, based on a hair treatment concept developedby Labo back in 1991 focusing on hair re-growth.

In 2011 the evolution of the formula (named HFSC) allowed to grant re-growth efficacy on 100% of the treated subjects.

In 2015 Labo developed the Transdermic Technology which certifies, through a scientific method, the percentage of active ingredients penetrating the skin tissues (epidermis and dermis) of skin and scalp.

In 2019 Labo added the Booster Complex to support the hair growth process and Cyclodextrins for a prolonged action of the ingredients.

2. Crescina Formulation Complexes

- Re-Growth Complex
- HFSC Complex
- Booster Complex
- Cyclodextrins

Formulation Complexes Contained in Crescina

The new Crescina Transdermic HFSC formulation is based on Labo's historical formula for thinning hair that includes:

The Re-Growth Complex (Cysteine, Lysine, Glycoprotein);

The HFSC Complex (Stem-Engine: Hydrolyzed Rice Protein, Corosolic Acid);

The Booster Complex (Methionine, Glycine, Copper Tripeptide-1)

Cyclodextrins for a prolonged action of the ingredients.

The Re-Growth Complex (Cysteine, Lysine, Glycoprotein)

Since 1998, Crescina Re-Growth formulation is based on a hydro-alcoholic solution in which are dispersed three active components that are essential to stimulate the physiological hair growth in the areas of the scalp affected by thinning.

In fact, Cysteine and Lysine are 2 amino acids among the main components of keratin, which is the protein that builds up the hair fibers and is produced inside the hair bulb by specialized cells, i.e. the keratinocytes.

The metabolism of these cells, especially in the quiescent bulbs, can slow down and therefore lead to deficiencies and abnormalities in the hair development and growth cycle. This is why the energy supply of the Glycoprotein helps improve the cell activity resulting in a greater protein synthesis by the keratinocytes.

The original formula also avails itself of the presence of Benzil Nicotinate, a vasodilator that increases blood microcirculation at scalp superficial level allowing a better supply of nutrients and a better oxygenation of hair bulbs and follicles, thus assisting the action of the functional molecules.

The basic Re-growth formulation is enriched also with Methionine sulfur amino acid and Octapeptide-2 peptide.

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The HFSC Complex (Stem-Engine: Hydrolyzed Rice Protein, Corosolic Acid)

In 2011 prof. Cotzarelis highlighted the essential role of bulge stem cells (a specific niche within the hair system) that are also present in the quiescent bulbs of patients suffering from baldness.

Since 2005, Labo researches have focused on the nature and potentialities of these matrix cells, responsible for the launch of the hair life cycles: the studies have finally brought to the development of the HFSC complex (Stem-Engine), consisting in Hydrolyzed Rice Protein and Corosolic Acid, which assists the physiological hair growth while maintaining the environment of the bulb's progenitor cells in good health to allow its proper development.

Thanks to this complex, Crescina HFSC formula obtained positive results in terms of regrowth in 100% of the treated volunteers, with a growth ranging from a minimum of + 7 to a maximum of + 41 new hairs per cm^2.

Swiss Patent CH 703 390

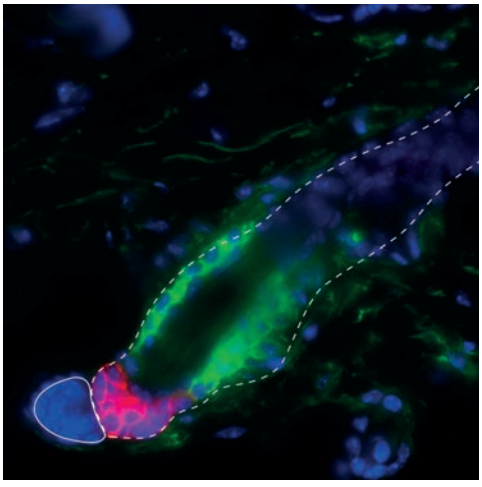


Photo of the follicle taken by means of a fluorescence microscope: green colour shows stem cells, while red colour shows the cells of the dermal papilla.

The Booster Complex

The Booster Complex included in Crescina Transdermic HFSC formulation has the function of providing the cells of the hair bulbs with molecules that will intervene at various levels and with different mechanisms of action in the hair growth process, consolidating the activities carried out by Re-Growth and HFSC complexes.

Methionine is an essential amino acid, meaning it is not produced by our body and must be introduced with food. It is necessary for the endogenous synthesis of cysteine and, just as cysteine, it is a source of sulfur, an indispensable element for the construction of hair keratin. Thanks to the presence of sulfur, it contrasts the free radicals and strengthens the hair.

Glycine contributes to the composition of the hair shaft in a percentage equal to 6.5%. It also plays an important role in collagen production which is necessary for hair growth. In fact, collagen represents about 70% of scalp dermis, that surrounds the hair follicles, and contributes to their structure, as well as to that of the dermal papilla.

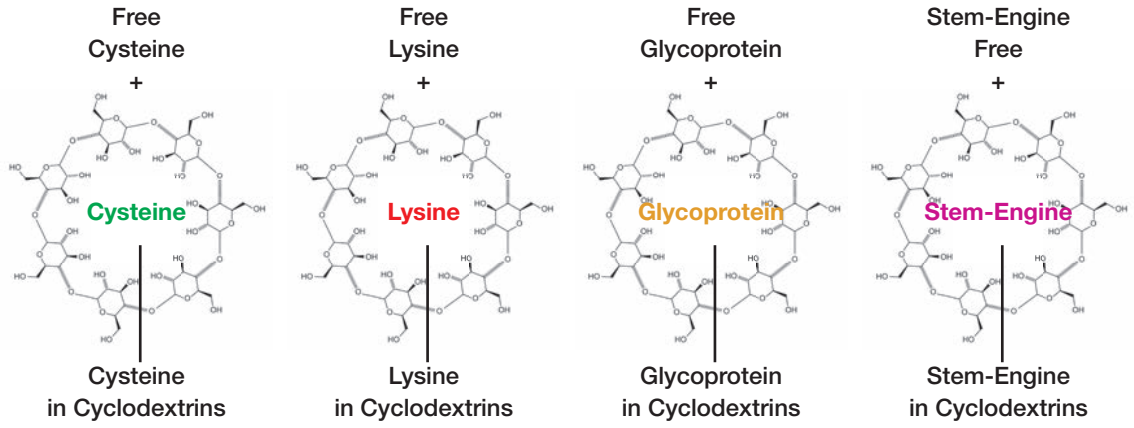
Copper Tripeptide-1 is a peptide that stimulates the proliferation of the fibroblasts of the dermal papilla, which are important in hair follicle morphogenesis and growth, and increases the production of VEGF, which stimulates the vascularization of the hair follicle. It promotes hair growth and hair thickness and increases the size of the follicle.

Cyclodextrins for a Prolonged Action

Cyclodextrins are molecular glucose rings that allow a gradual release of the active ingredients inserted within their structure.

In Crescina formulation, the molecules of the Re-Growth complex (Cysteine, Lysine, Glycoprotein) and of the HFSC complex (Stem-Engine) are present both in free form and conveyed in special Cyclodextrins: they release their content on the scalp constantly for more than 24 hours, granting a beneficial prolonged action.

Swiss Patent CH 693 815



SWISS PATENT CH 703 390

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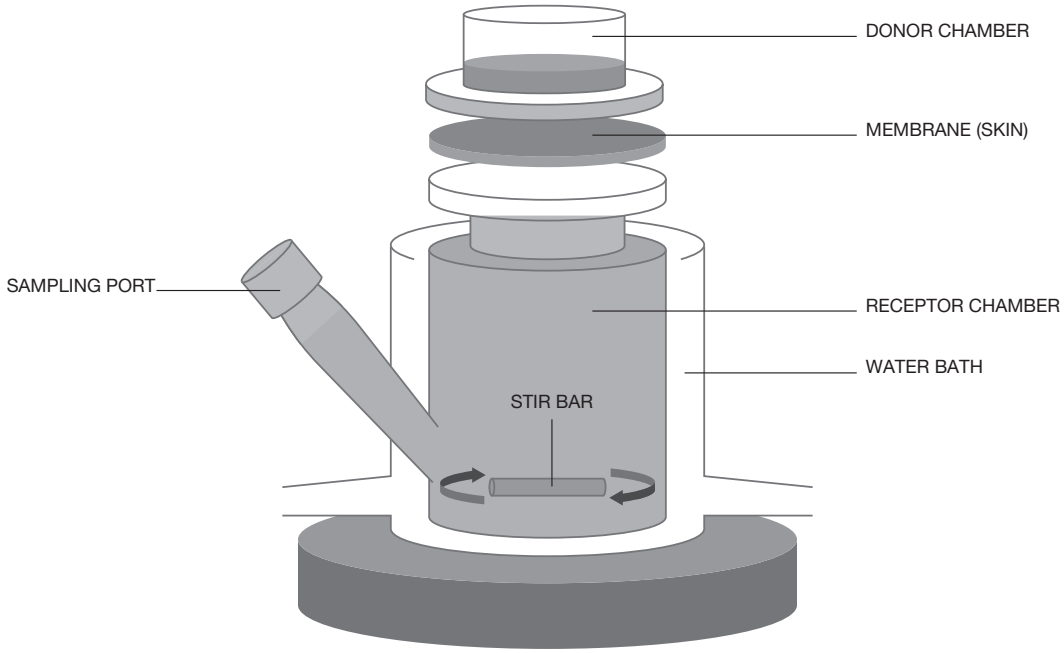
3. Transdermic Technology

Swiss Patent
CH 711 466



Scheme of a Franz Diffusion Cell

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Penetration Efficacy Thanks to Labo Patented Transdermic Technology

Labo patented Transdermic Technology (Swiss Patent CH 711 466) allows for the active and functional ingredients contained in the formulations **to penetrate the different layers of skin and scalp** - epidermis and dermis - and reach in a safe and proven way the deepest layers of the skin where they need to act: a real alternative to micro-injections, but without needles.

Transdermic Technology is mainly based on the molecular weight of the active substances that, in association with specific enhancers, guarantees the best penetration not only through the follicular opening, but also through the thicker and hardly accessible skin layers of the entire scalp.

Transdermic Technology is fundamental for the efficacy of the treatment: without it, it would not be possible to obtain the penetration and the activity results that are normally obtained with the micro-injections.

Therefore, Transdermic Technology makes Crescina preparation unique: no other topical product can claim **a tested and controlled transdermic activity with *ex vivo* verified percentages** of the penetration values.

The 12 “synthetic human” molecules of the new Plate-Like Complex can count on low and very low molecular weights. Their penetration has been tested by means of Franz Diffusion Cells.

Chart: Transdermic Penetration Percentages of the Active Ingredients of Crescina Transdermic HFSC

HFSC Complex – 2 Molecules

Hydrolyzed Rice Protein	Corosolic Acid	
3.500 (Da)	472,70 (Da)	*Molecular weight (in dalton)*
84,40%	76,90%	*Penetration % Epidermis + Dermis*

Regrowth Complex – 3 Molecules

Acetyl Cysteine	Lysine HCl	Glycoproteins	
163,19 (Da)	146,19 (Da)	20.000 (Da)	*Molecular weight (in dalton)*
56,70%	58,30%	82,40%	*Penetration % Epidermis + Dermis*

Booster Complex – 3 Molecules

Methionine	Glycine	Copper Tripeptide-1	
149,20 (Da)	75,07 (Da)	404,00 (Da)	*Molecular weight (in dalton)*
52,30%	75,90%	77,00%	*Penetration % Epidermis + Dermis*

Note: The percentages reported here above refer to the transdermic penetration of the functional active molecules, in solution, after 24 hours. Transdermic penetration was made possible thanks to the new Labo technology and tested by means of Franz Cells.

4. Crescina: The Product

Difference Between Hair Loss and Hair Thinning

HAIR **LOSS**

Detachment of a hair
from its natural site (the follicle)

ANTI-HAIR LOSS PRODUCT

Anti-hair loss products act on the elasticization of the walls and on the anchoring of the bulb to the follicle, **stopping the premature detachment of the hair.**

HAIR **THINNING**

Lack of hair re-growth

CRESCINA RE-GROWTH

Crescina Re-Growth is the first treatment able to act on the reactivation of regrowth processes on non-atrophied bulbs, **supporting the physiological hair regrowth.**

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Crescina Concept: Thinning Hair vs Hair Loss

To understand the unique quality of Crescina Re-Growth, it is important to distinguish between the problem of **hair loss** and the problem of **thinning of the scalp**.

Hair loss is an evolving phenomenon, represented by the detachment of a hair from its seat, the hair follicle. People who suffer from hair loss make statements such as: “I find a lot of hairs on my comb, brush, and shoulders when I comb or brush my hair, on the pillow when I sleep, in the sink on the shower plate when I wash my hair etc.”.

Whereas, **thinning** is an actual condition caused by the lack of hair regrowth after it has fallen out (even if not observable) that manifests itself in lower hair density in specific areas of the scalp defined as “thinned areas”.

People who notice hair thinning, say things like: “I see empty spaces between the hairs, bald patches have formed, I no longer have thick hair like I used to etc.”.

Anti-hair loss treatments aim at stopping the detachment of existing hair. Crescina Re-Growth promotes the physiological hair growth in areas affected by thinning.

For this reason, in addition to the **re-growth formulation** for thinning hair acting specifically on the bulbs.

"Thinometer" with male and female scale of thinning and the corresponding dosages of Crescina.

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Crescina Concept: Dosages

Crescina scale of thinning and dosages

Crescina Re-Growth was initially developed with specific dosages for thinning stages in order to better deal with the various needs for treating thinning and incipient baldness. In fact, this phenomenon evolves with a progression that is well represented by the international Hamilton Scale for men and Ludwig Scale for women.

In 2010, Labo updated the Hamilton scale following Norwood studies (Savin is for women).
This broader male scale consists of 12 stages of thinning, the first 8 of which can be treated with Crescina Re-Growth.
These eight stages (and the 5 stages of the female scale) have been grouped into three sets: initial stages, medium stages, advanced stages. The concentrations of Crescina Re-Growth refer to these sets.

Dosage 200 for initial grades (moderate thinning hair in men or women)

Dosage 500 for medium grades (advanced thinning hair in men or women)

Dosage 1300 for advanced grades (incipient baldness in men or women)

The photographic scale of hair thinning called “Thinometer” helps to choose the correct dosage for your condition.

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Crescina Transdermic HFSC The Products

Crescina Transdermic HFSC

For Hair Regrowth

Crescina Transdermic Re-Growth HFSC is a topical dermo-cosmetic preparation to help promote the physiological hair growth, whose formula benefits from Labo Transdermic Technology: the active molecules can thus penetrate into the hair system not only via trans-follicular route (through the follicle opening) but also transdermally (ex vivo test with Franz Cells), i.e. through the skin layers of the scalp (epidermis and dermis). Thanks to their low molecular weight and to the presence of enhancers, the functional active ingredients are facilitated in their penetration and in their performance (see table with the results of the penetration test reported on top of the box).
The formulation contains: the Re-Growth Complex (Cysteine, Lysine, Glycoprotein), the HFSC Complex (Stem-Engine), the new re-growth booster complex (Methionine, Glycine, Copper Tripeptide-1), 3 enhancers (Pentylene Glycol, Decylene Glycol, Caprylyl Glycol).

Specific formulae for Man and Woman. Recommended in cases of thinning due to physiological - not pathological - causes. Does not act on completely atrophied hair follicles. Available in 20-vial boxes and in the following dosages: 200, 500, 1300.

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Crescina Transdermic HFSC The Products

Crescina Transdermic HFSC Complete Treatment

For Hair Regrowth and for Hair Loss

Crescina Transdermic HFSC Complete Treatment is a topical dermo-cosmetic treatment in vials with double function: it helps the physiological hair growth and helps stop the hair-loss.

The packaging contains two vial types: amber vials contain **Crescina Transdermic Re-Growth HFSC** while transparent vial contain **Crescina Transdermic Anti-Hair Loss**, combining the basic active ingredients (Hydroxyproline, Aspartic Acid, Enzymatic Activator and Taurine) with Hydrolyzed Yeast Protein and Acetyl Tetrapeptide-3, helpful to reinforce hair from the root (in vitro test on the active ingredients), plus 3 enhancers to facilitate their penetration (Transdermic Technology) through both hair system and scalp. The formulation is enriched with the HSSC Complex.

Specific formulae for Man and Woman. Available in 10+10-vial boxes and in the following dosages: 200, 500, 1300.

Crescina®
Transdermic
Re-Growth
HFSC
(amber vials)

Crescina®
Transdermic
Anti-Hair Loss
(transparent vials)

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Crescina Transdermic HFSC The Products

Crescina Transdermic HFSC

HOW TO USE

The preparation is contained in 3,5ml single-dose vials to be applied daily for 5 consecutive days, followed by a two-day break (e.g. from Monday to Friday, with a break on Saturday and Sunday). Apply Crescina Re-Growth onto a clean, dry scalp. Recommended application time: minimum 2 month.

APPLICATION SCHEME

CRESCINA® TRANSDERMIC RE-GROWTH HFSC

It helps promote the physiological hair growth. 100% Formula

	M	T	W	T	F	S	S
WEEK 1						–	–
WEEK 2						–	–

Repeat this order until the pack is finished. See internal leaflet.

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Crescina®
Transdermic
Re-Growth
HFSC
3,5 ml

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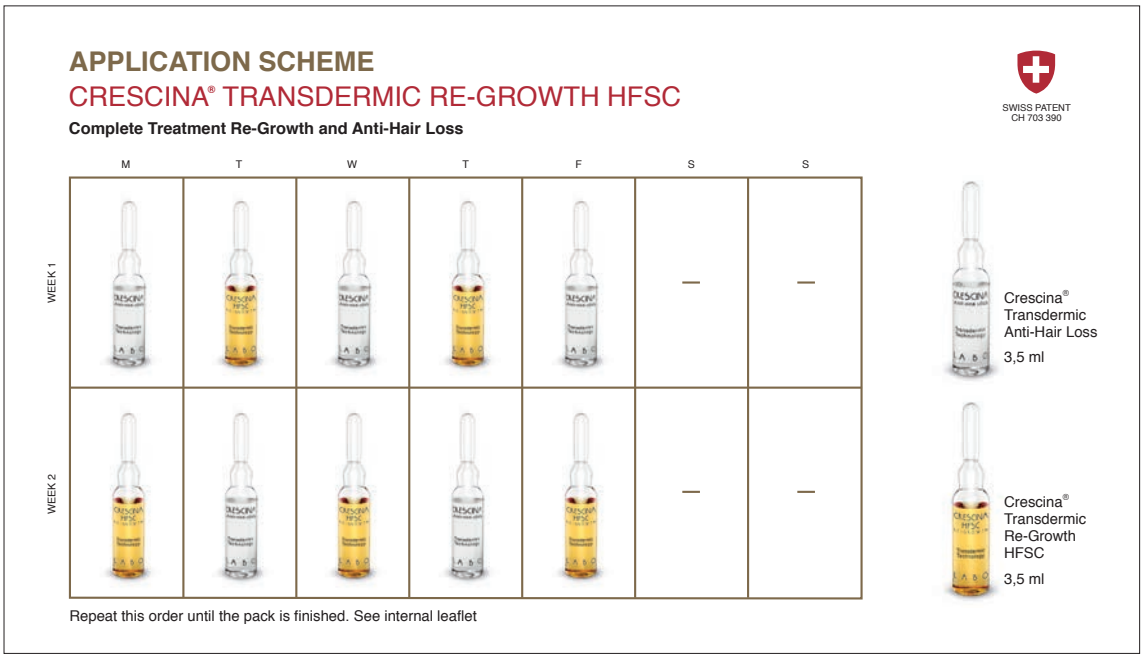
Crescina Transdermic HFSC The Products

Crescina Transdermic HFSC Complete Treatment

HOW TO USE

In this case, the treatment begins with the anti-hair loss vial (transparent vial), followed by the re-growth vial (amber vial) on the next day, according to the table below.



5. Efficacy Studies on Crescina

Efficacy Studies on Crescina

To The cosmetic activity performed by Crescina which aids hair regrowth in thinning areas is documented by numerous *in vivo* and *in vitro* clinical and instrumental efficacy tests:

1. Clinical study for evaluating the activity of a trichological lotion in subjects affected by thinning due to androgenetic alopecia and/or defluvium. E3398/A - May 1999.

2. Clinical study for evaluating the activity of a trichological lotion in subjects affected by thinning due to androgenetic alopecia and/or defluvium. E1599/B – February 2001.

3. *In vitro* evaluation of the stimulating activity induced by a cosmetic preparation for the treatment of hair thinning on human fibroblasts and keratinocytes. REL552/04/MIT/ELB – July 2004.

4. *In vitro* evaluation of the stimulating activity induced by a cosmetic preparation for the treatment of hair thinning on human fibroblasts and keratinocytes. REL173/05/MIT/ELB – June 2005.

5. Effects of Crescina on human primary epidermal and dermal cells. Effects of Crescina on fibroblasts/keratinocytes – July 2005.

6. Assessment in humans of the effect on hair re-growth of a hair lotion after application under normal conditions of use. Checking of acceptability. Use test under dermatological control with objective assessment of the efficacy. II345/05.1490 and 05.1491 – May 2006.

7. Evaluation of the activity, cosmetic qualities and skin tolerability of a cosmetic lotion for hair regrowth. 06-34 – November 2006.

Efficacy Studies on Crescina

8. Evaluation of the activity, cosmetic qualities and skin tolerability of a cosmetic lotion for physiological hair regrowth and increased hair thickness. 06-73 – May 2007.

9. Effects of Crescina Re-Growth on the diameter of human hair follicles (*ex vivo*). GT070627 – August 2007.

10. Evaluation of the efficacy of a cosmetic product in facilitating physiological hair regrowth and promoting the increase of hair thickness. 08/17 – July 2008.

11. Evaluation of the efficacy and the cosmetic quality of an active lotion in facilitating physiological hair regrowth, under normal conditions of use, and after 90 consecutive days of use. 09-19 – July 2009.

12. *In vitro* study on hair follicle stem cells. LB_0511_3_II – July 2011.

13. Efficacy study of Crescina Re-Growth. Self-assessment test – March 2012.

14. Efficacy study of Crescina Re-Growth HFSC. Self-assessment test – April 2012.

15. Clinical-Instrumental, double blind, randomised, placebo-controlled study on the efficacy of a cosmetic lotion, Crescina HFSC, to aid hair growth in thinning and bald areas. F.U.05.C.L_2011/2192 – April 2012.

16. *Ex vivo* evaluation of the absorption potential of the aminoacids, vitamins, oligoelements and nucleic acids contained in a mix through the skin (epidermis + dermis). TV.01.C_2014/3129 – March 2015.

17. Evaluation of the efficacy and tolerability of a hair cosmetic treatment helping hair growth in the thinning areas, through clinical-instrumental test, double-blind and placebo controlled (Women). 1405 G16F – April 2015.

Efficacy Studies on Crescina

18. *In vitro* evaluation of the absorption potential of the following cosmetic active molecules through the skin (epidermis + dermis). TV.01.C_2015/1914 – October 2015.

19. *In vitro* evaluation of the absorption potential of the following cosmetic active molecules (N-Acetyl Cysteine, Lysine HCl, Glycoproteins, Methionine, Octapeptide-2, Hydrolyzed Rice Protein, Eriobotrya Japonica Leaf Extract) through the skin (Epidermis+Dermis) in presence of an enhancer mixture composed by 3 cosmetic helpers. TV.01.C_2015/3266. March 2016.

Efficacy Studies on Crescina

E3398/A – MAY 1999

1. Clinical study for evaluating the activity of a trichological lotion in subjects affected by thinning due to androgenetic alopecia and/or defluvium.

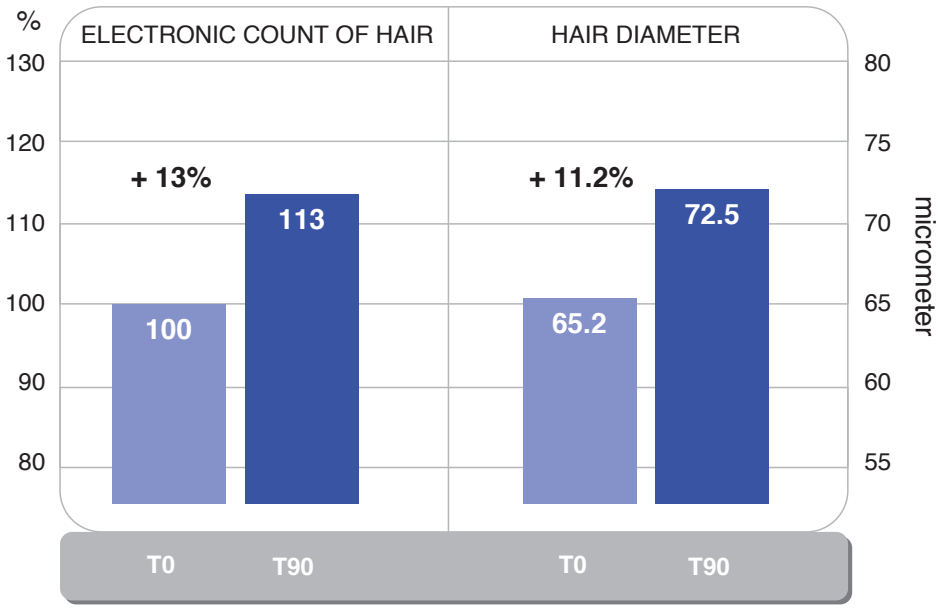
The study was conducted on a group of 25 volunteers, 14 female and 11 male, between 23 and 45 years of age, affected by androgenetic alopecia classifiable as stage I-II on the Ludwig scale in the case of the women, and stage II-III on the Hamilton scale for the men, and/or by defluvium. During the study subjects were asked to apply Crescina on alternate days for a period of 90 days. Before the start (T0) and at the end of the test (T90) a small area has been shaved and photographed for electronic hair count. The measurements and clinical evaluations have been performed in order to establish, within general parameters, the status of the hair bulbs before and after the test, as well as the status of the hair shafts (diameter or thickness increase).

After three months of treatment the tests show a statistically significant increase of 13% in growing hair, compared to baseline value, measured by digital count. Observation of the hair bulbs under the optical microscope showed, after three months of treatment, an increased proportion of bulbs in the anagen phase, i.e. a growth of new hair from 3,7% to 25,9% and a reduced proportion of bulbs in the telogen phase (rest and hair loss) from 81,5% to 57,7%. The morphometric analysis of enlarged hair images, has revealed an average increase of 11,2% in diameter (thickness of the shaft), after a treatment of three months.

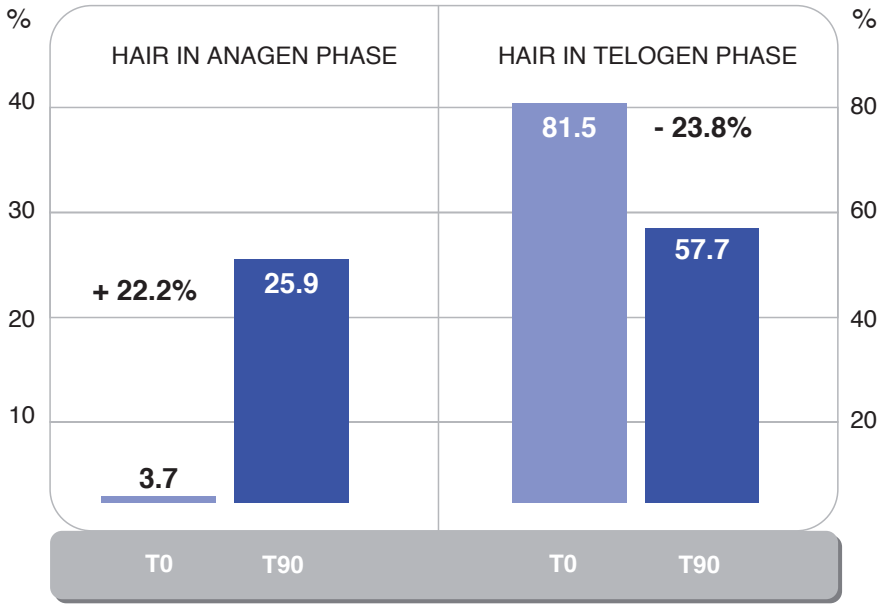
Efficacy Studies on Crescina

E3398/A – MAY 1999

Crescina Re-growth – Clinical Test E3398A



Crescina Re-growth – Clinical Test E3398A
Morphology of the bulb



Efficacy Studies on Crescina

E1599/B – FEBRUARY 2001

2. Clinical study for evaluating the activity of a trichological lotion in subjects affected by thinning due to androgenetic alopecia and/or defluvium.

The test was conducted on a group of 42 subjects who utilized Crescina Re-Growth composed of 24 female, 18 male affected by varying degrees of alopecia: Ludwig stage I-II in female subjects, Hamilton stage II-III-IV-V in males and/ or defluvium. A phototrichogram was performed in baseline conditions (T0), at two months (T2), and at three months (T3).

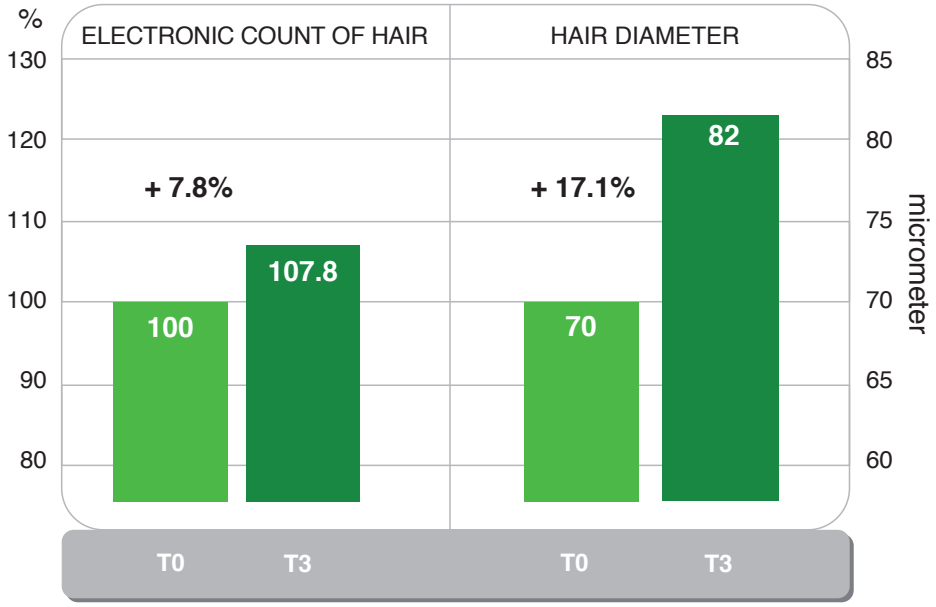
The photos have been analysed for electronically counting the number of hairs, the percentage of hairs in the anagen (growth) and telogen (rest) phases, and for measuring the hair diameter.

A statistically significant increase of hair in anagen phase was noticed: from 27 to 53% i.e. an increase of 26% after 90 days. After three months of treatment the tests show a significant increase of +7,8% in growing hair, compared to baseline value, measured by digital count. The average hair diameter increases by 17% after 90 days of treatment.

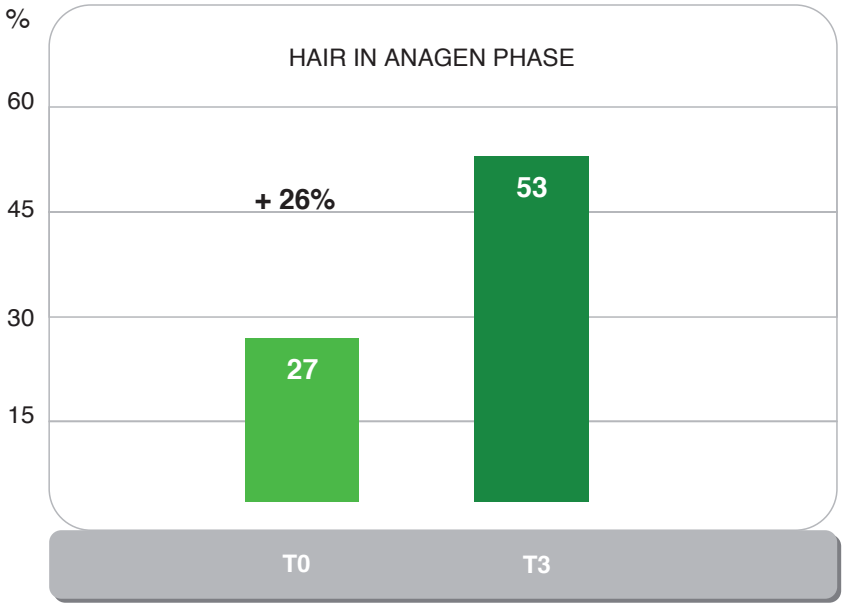
Efficacy Studies on Crescina

E1599/B – FEBRUARY 2001

Crescina Re-growth – Clinical Test E1559/B



Crescina Re-growth – Clinical Test E1599/B
Morphology of the bulb



Efficacy Studies on Crescina

REL552/04/MIT/ELB – JULY 2004

3. *In vitro* evaluation of the stimulating activity induced by a cosmetic preparation for the treatment of hair thinning on human fibroblasts and keratinocytes.

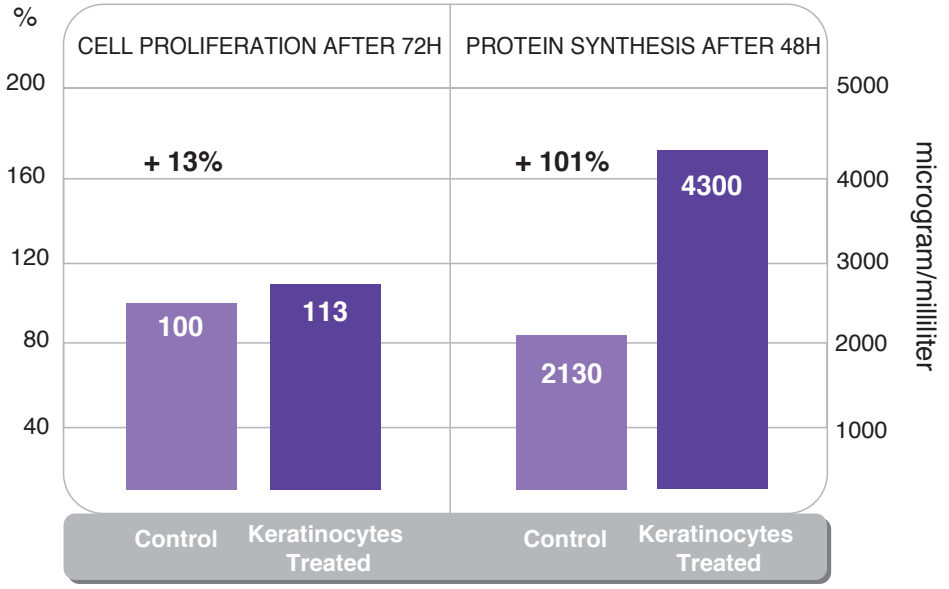
The preparation Crescina Re-Growth is very effective in stimulating the human skin-derived fibroblasts, typical cells that in the dermis are aimed to the hair papilla development. The product is very effective in stimulating the protein neosynthesis, in particular in the keratinocytes, cells that are aimed to the keratin synthesis.
We have pointed out a clear effect on fibroblasts proliferation after 24h as well as after 48h and after 72h compared to untreated cells, even with the lower tested dosages. We have pointed out a quite moderate increase in keratinocytes proliferation (+13%) with the tested products. In treated fibroblasts the cell proliferation is up to +55% in 24h with the product Crescina Re-Growth.

The preparation Crescina Re-Growth stimulates in a more intensive way the total protein synthesis in keratinocytes (+101%) compared to fibroblasts (+12%) after 48h of treatment following exposure at the 5mg/ml concentration of the preparation.

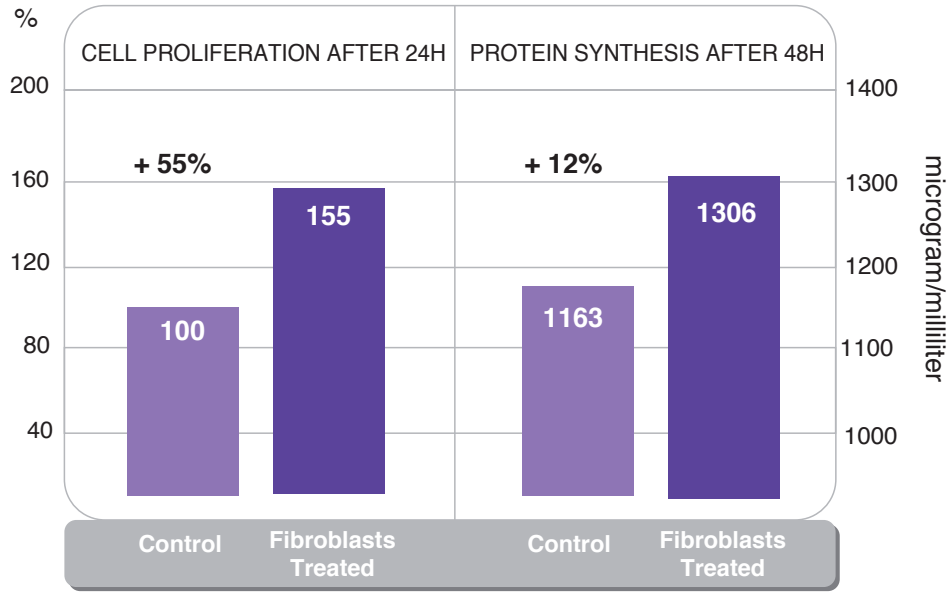
Efficacy Studies on Crescina

REL552/04/MIT/ELB – JULY 2004

Crescina Re-Growth – *In vitro* test
Keratinocyte culture



Crescina Re-Growth – *In vitro* test Abich
Fibroblasts culture



Efficacy Studies on Crescina

REL173/05/MIT/ELB – JUNE 2005

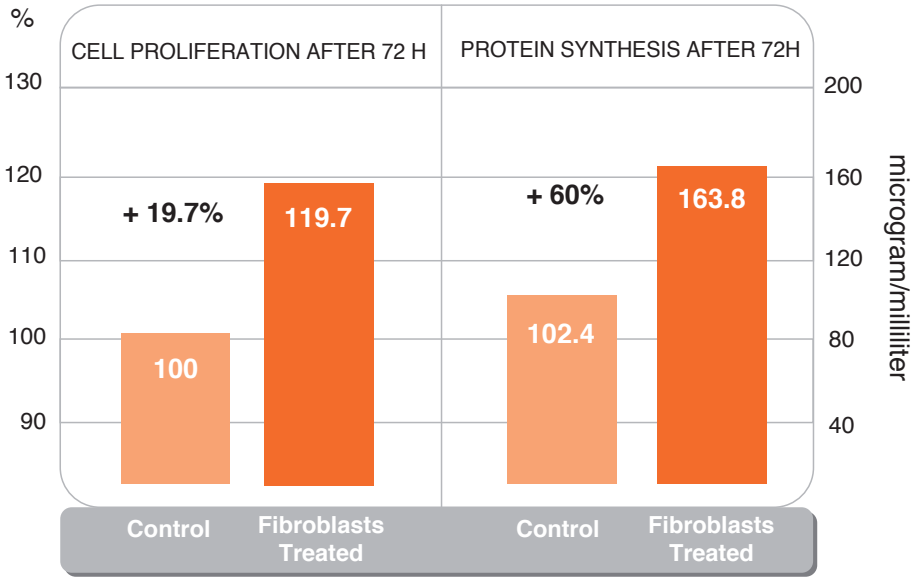
4. *In vitro* evaluation of the stimulating activity induced by a cosmetic preparation for the treatment of hair thinning on human fibroblasts and keratinocytes.

Following exposure at serial concentrations of the product Crescina Re-Growth the cell proliferation has been evaluated after 24, 48 and 72h and calculated as cell vitality in percentage respect to untreated cells. This test was performed using two cell lines: fibroblasts and keratinocytes.
On keratinocytes, at the tested time 48 and 72h we have pointed out a clear effect of cell proliferation (values > 100% cell vitality), compared to untreated cells (cell vitality considered as 100%). The effect was especially evident after 72h with 1,25 mg/ml concentration, with an increase in cell proliferation of 55,4% vs control cells.
On fibroblasts we have pointed out the maximun proliferation after 72h: +19,7% compared to the untreated cells. Protein quantification was performed on both cell lines: fibroblasts and keratinocytes. The test performed using fibroblasts, detect an increase in the total protein content compared to untreated cells up to 60% for the highest tested doses after 72h exposure. The test performed on keratinocytes shows an high increase in protein synthesis compared to untreated cells, with its peak after 72h, about + 61% with a 0,63 mg/ml sample concentration.

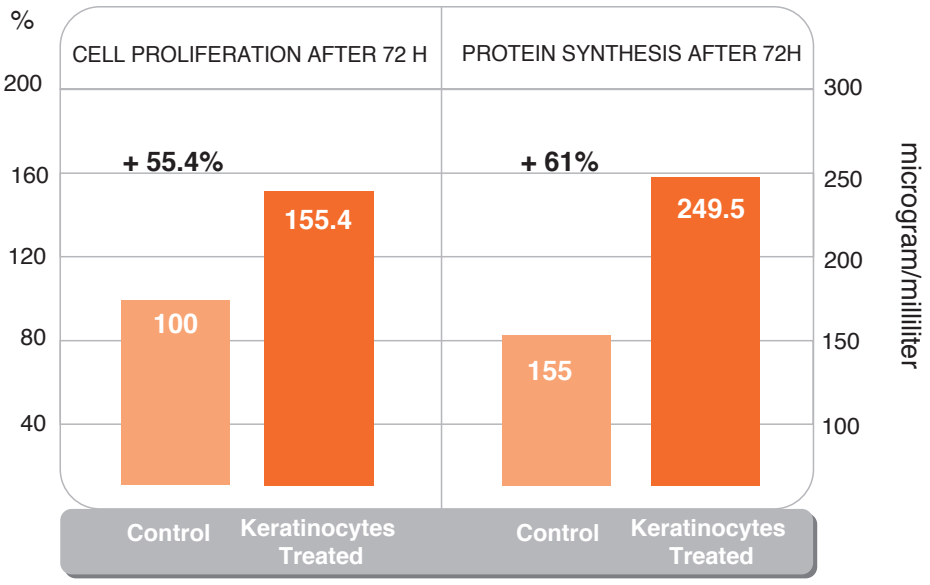
Efficacy Studies on Crescina

REL173/05/MIT/ELB – JUNE 2005

Crescina Re-Growth – *In vitro* test
Fibroblasts Culture



Crescina Re-Growth – *In vitro* test
Keratinocyte culture



Efficacy Studies on Crescina

EFFECTS OF CRESCINA ON FIBROBLASTS/KERATINOCYTES – JULY 2005

5. Effects of Crescina on human primary epidermal and dermal cells.

Objective: To establish quantitatively the effectiveness of the product tested on the cell proliferation and on the increase of the total proteins' content.

An aqueous solution containing the core ingredients of Crescina (Glycoprotein and amino acids Lysine and Cysteine) was tested in order to determine:
1) proliferation of primary keratinocyte and fibroblast cells
2) protein synthesis of primary keratinocyte and fibroblast cells

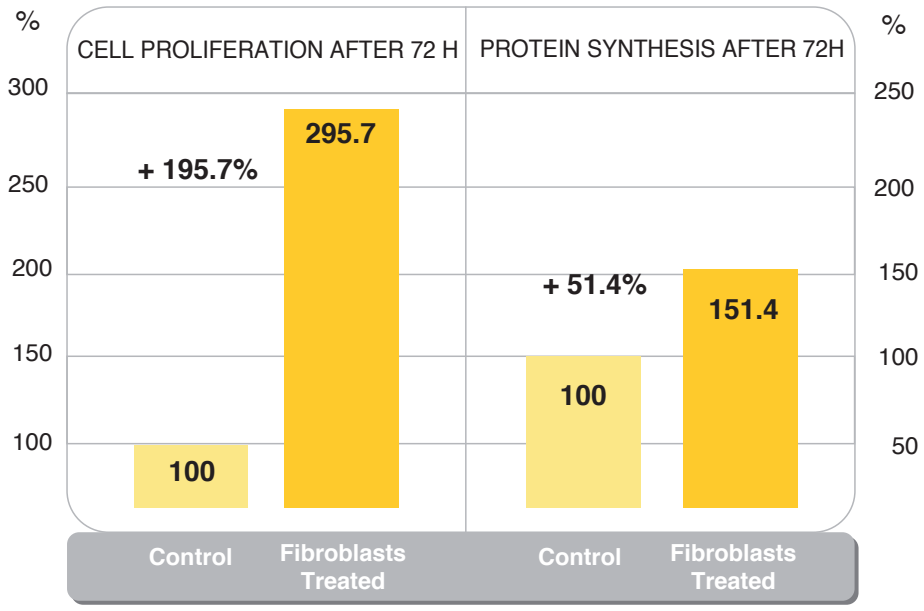
Determination of cell proliferation
In the case of keratinocyte cultures, the AlamarBlue assay showed an increase in cell vitality, not observed in untreated cells, at the different test intervals (+54.8%, +56.3% and +61.6% after 24, 48 and 72 hours treatment, respectively, with the Crescina solution). Findings suggest that Crescina increases metabolic activity of the cells, raising the level of cellular energy.
In the case of fibroblast cultures, the AlamarBlue assay showed an increase in cell metabolism, not observed in untreated cells, at the different test intervals of 24, 48 and 72 hours (maximal values observed: +58.5% after 24 hours; +111.4% after 48 hours; +195.7% after 72 hours).

Determination of protein content
In the case of keratinocyte cultures, the BCA method showed an increase in the protein content of treated cells, not observed in untreated cells (maximal values observed: +160.3% after 24 hours; +242.1% after 48 hours and +73.9% after 72 hours in Crescina solution).
A slight increase in protein content was visible in fibroblasts after 72h: +51.4% with esposition at 0.125% of Crescina.

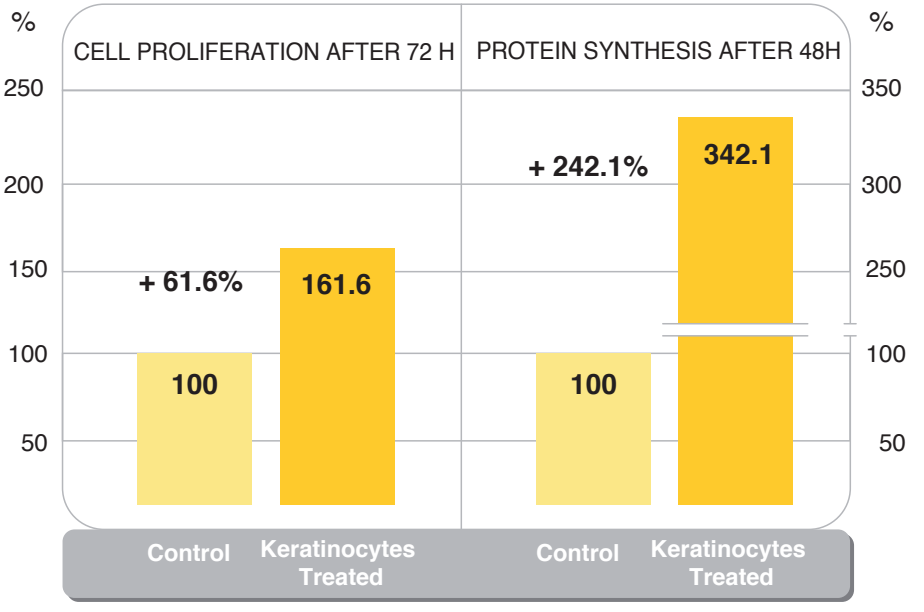
Efficacy Studies on Crescina

EFFECTS OF CRESCINA ON FIBROBLASTS/KERATINOCYTES – JULY 2005

Crescina Re-Growth – *In vitro* test
Fibroblasts Culture



Crescina Re-Growth – *In vitro* test
Keratinocyte culture



Efficacy Studies on Crescina

IL 345 / 05.1490 AND 05.1491 – MAY 2006

6. Assessment in humans of the effect on hair re-growth of a hair lotion after application under normal conditions of use. Use test under dermatogical control with objective assessment of the efficacy.

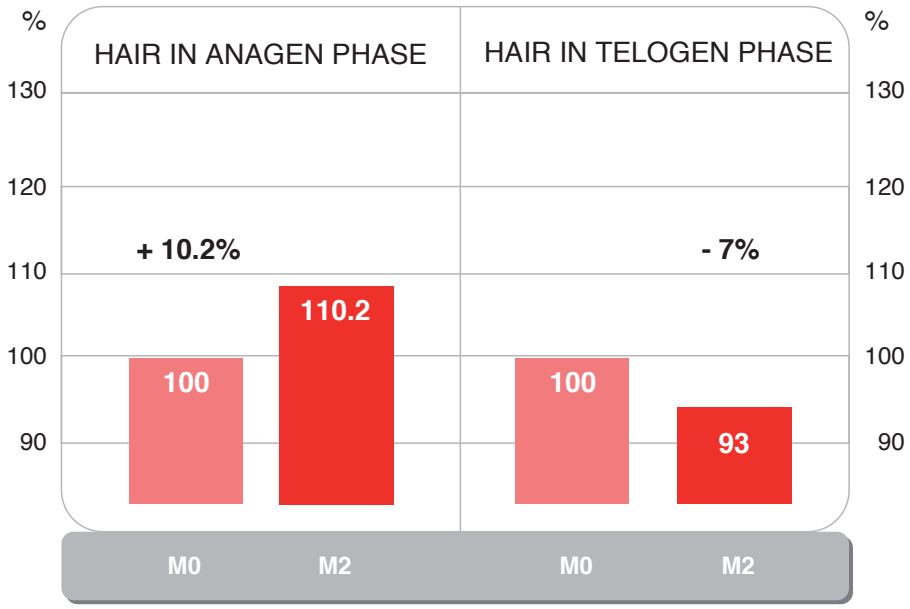
The test involved 18 volunteers who agreed to use Crescina Re-Growth in accordance with directions given by Labo. The volunteers were male, aged between 20 and 55 years and affected by androgenetic alopecia stages II to IV (corresponding to stages I – VII on the Hamilton-Norwood scale). Efficacy was evaluated by the phototrichogram method.
A phototrichogram was performed initially in baseline conditions (M0), then after 56 days (M2) and after 84 days (M3) following the start of the treatment.

- Findings reveal a significant increase in the number of anagen phase hairs: +10.2% after 56 days of treatment.
- A significant reduction in the number of telogen phase hairs was recorded: - 7% after 56 days of treatment.
- 78% of the volunteers after 2 months' treatment and 71% of the volunteers after 3 months' treatment showed an increase in percentage of hair in anagen phase.
- 57% of the volunteers after 2 months' treatment and 71% of the volunteers after 3 months' treatment showed an increase in hair density.

Efficacy Studies on Crescina

IL 345 / 05.1490 AND 05.1491 – MAY 2006

Crescina Re-Growth – *In vivo* test
Phototrichogram



Efficacy Studies on Crescina

06-34 – NOVEMBER 2006

7. Evaluation of the activity, cosmetic qualities and skin tolerability of a cosmetic lotion for hair regrowth.

This study aimed at evaluating the activity, in normal conditions of use, of a cosmetic lotion for hair regrowth called “Crescina Re-Growth”.
Hair regrowth was evaluated with the photo-trichogram technique, performed at baseline, after 60 days and 90 days of treatment. This technique was performed on an area of the scalp affected by alopecia, on which a side area of 1 cm was carefully marked with tattooed dots (removable at the end of the test).

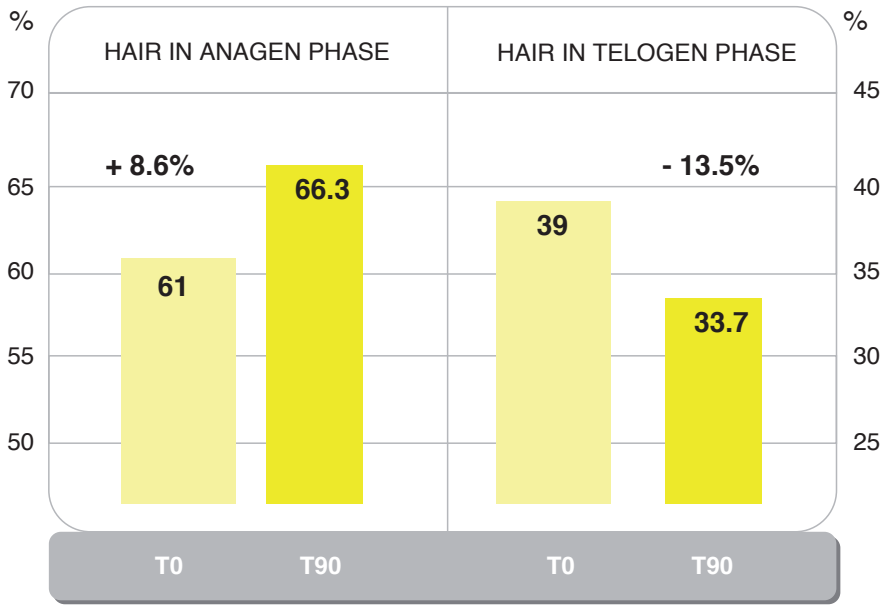
For each experimental time were calculated:
- the total number of hairs
- the number of hairs in the anagen phase
- the number of hairs in the telogen phase

The results obtained after 90 days of treatment showed that the tested product:
- induced a 2.74% increase in the total number of hairs
- induced an 11.78% increase in the number of hairs in the anagen phase
- induced an 11.40% reduction in the number of hairs in the telogen phase
- induced an 8.67% increase in the percentage of hairs in the anagen phase
- induced a 13.56% reduction in the percentage of hairs in the telogen phase

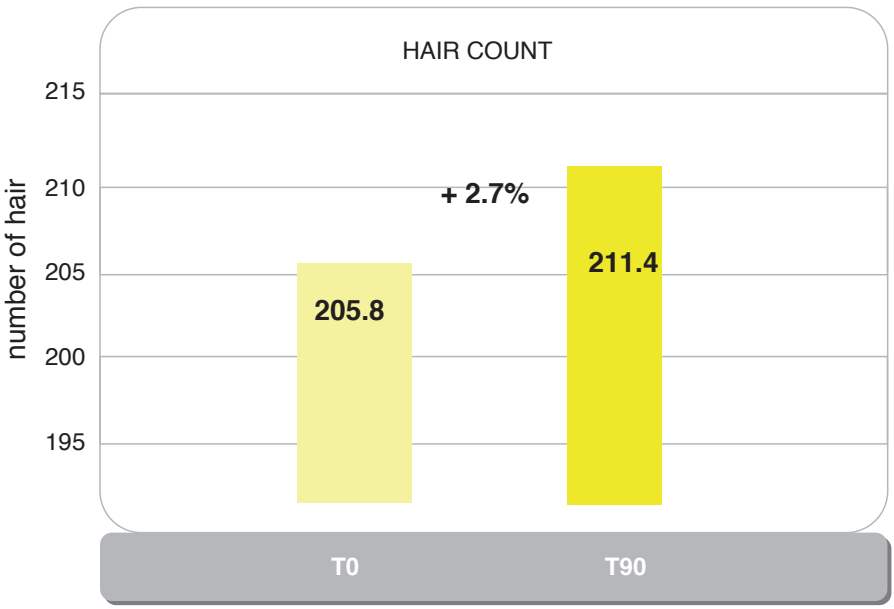
Efficacy Studies on Crescina

06-34 – NOVEMBER 2006

Crescina Re-Growth – *In vivo* test
Phototrichogram



Crescina Re-Growth – *In vivo* test
Phototrichogram



Efficacy Studies on Crescina

06-73 – MAY 2007

8. Evaluation of the activity, cosmetic qualities and skin tolerability of a cosmetic lotion for hair regrowth and increased hair thickness.

25 volunteers were included in the test, men and women aged between 35 and 60 years with androgenetic alopecia (stage II and III on the Hamilton scale for men and stage I and II on the Ludwig scale for women).
Hair growth was evaluated with the phototrichogram technique, performed at baseline, after 60 days and 90 days of treatment.
10 hairs were cut during the phototrichogram at baseline and after 90 days of treatment and analysed to measure the hair shaft diameter.

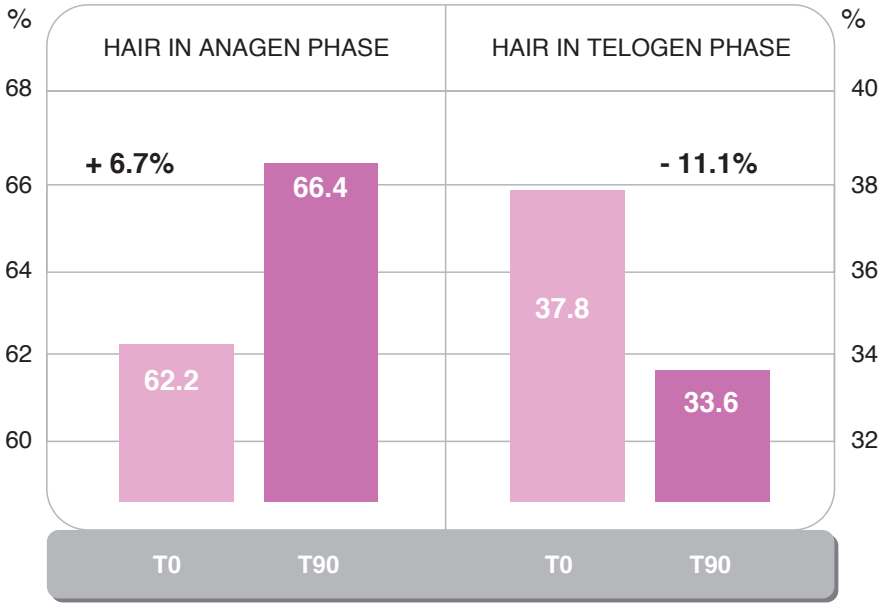
The results obtained after 90 days of treatment showed that the tested product:
- induced a 2,61% increase in the total number of hairs
- induced a 9,32% increase in the number of hairs in the anagen phase
- induced a 8,54% reduction in the number of hairs in the telogen phase
- induced a 6,75% increase in the percentage of hairs in the anagen phase
- induced an 11,11% reduction in the percentage of hairs in the telogen phase

The results obtained showed that the treatment induced a 2,41% increase in the diameter of the hair shaft after 90 days of treatment.

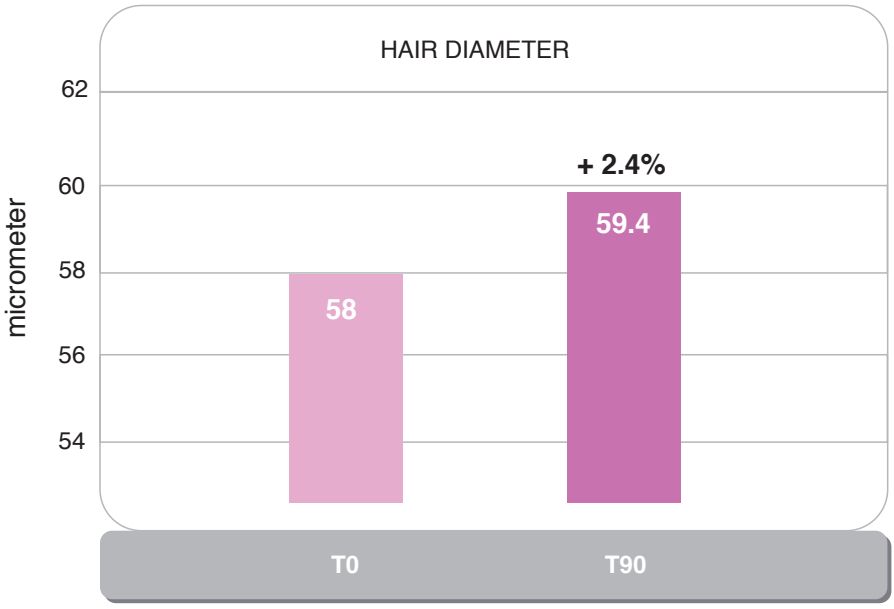
Efficacy Studies on Crescina

06-73 – MAY 2007

Crescina Re-Growth – *In vivo* test
Phototrichogram



Crescina Re-Growth – *In vivo* Test



Efficacy Studies on Crescina

GT070627 – AUGUST 2007

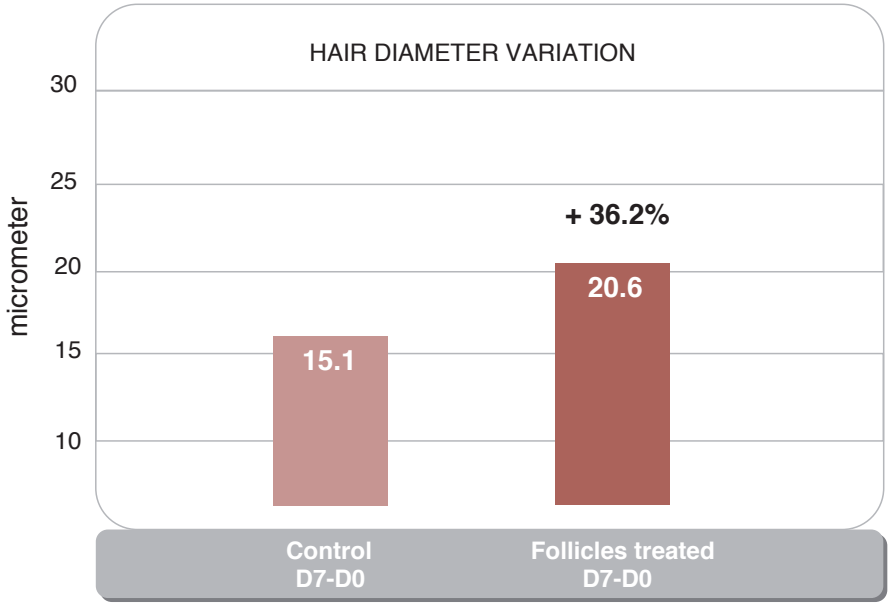
9. Effects of Crescina Re-Growth on the diameter of human hair follicles (*ex vivo*).

It has been tested a preparation formed by the nucleus of Crescina hair treatment and other active principles characterising Crescina Re-Growth with the following composition: aqua, glycerin, lysine hydrochloride, acetyl cysteine, glycoproteins, caffeine, silanediol salicylate, glucose, serine, threonine, tetrasodium disuccinoyl cystine, zinc acetylmethionate, glycine, arginine, Eriobotrya japonica leaf extract, apigenin, oleanoic acid, biotinoyl tripeptide-1. Labo performed this study in order to find evidence of possible effects on hair thickness in an experimental assay using human hair follicles obtained from human skin fragments (fronto-temporo-facial lifting) by microdissection. The diameter of the hair root was analyzed at various times.
The hair follicles were cultivated in William culture medium containing or not (control) the test compound. The diameter of each hair was measured at day 7. After 7 days of contact, Crescina Re-Growth tested at 0.5% revealed to increase the hair follicles thickness of +36% compared to not-treated follicles (negative control).

Efficacy Studies on Crescina

GT070627 – AUGUST 2007

Crescina Re-Growth – Ex vivo test
Human follicles culture after 7 days



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Efficacy Studies on Crescina

08-17 – JULY 2008

10. Evaluation of the efficacy of a cosmetic product in facilitating physiological hair regrowth and promoting the increase of hair thickness.

This study aimed at evaluating the efficacy of a cosmetic product called “Crescina Re-Growth”, in facilitating physiological hair regrowth and promoting the increase of hair thickness.
The efficacy was evaluated with the phototrichogram technique, performed at baseline, after 60 days and 90 days of treatment.

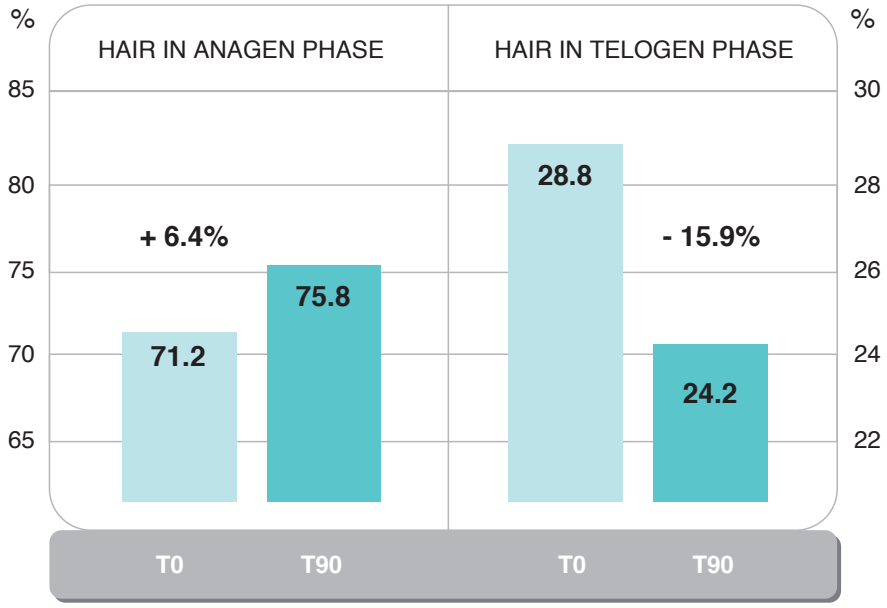
20 volunteers were included in the test, 10 men and 10 women aged between 35 and 60 years with mild androgenetic alopecia (stage II and III on the Hamilton scale for men and stage I and II on the Ludwig scale for women).
The results obtained after 90 days of treatment showed that the tested treatment:
- induced a 6.98% increase in the number of hairs in the anagen phase
- induced a 15.53% reduction in the number of hairs in the telogen phase
- induced a 6.45% increase in the percentage of hairs in the anagen phase
- induced a 15.95% reduction in the percentage of hairs in the telogen phase

The results obtained showed that the treatment induced a 1.74% increase in the diameter of the hair shaft after 60 days of treatment, and a 2.09% increase after 90 days of treatment.
Based on the results obtained in this study, we can say that Crescina Re-Growth showed good cosmetic efficacy in facilitating physiological hair regrowth and promoting the increase of hair thickness.

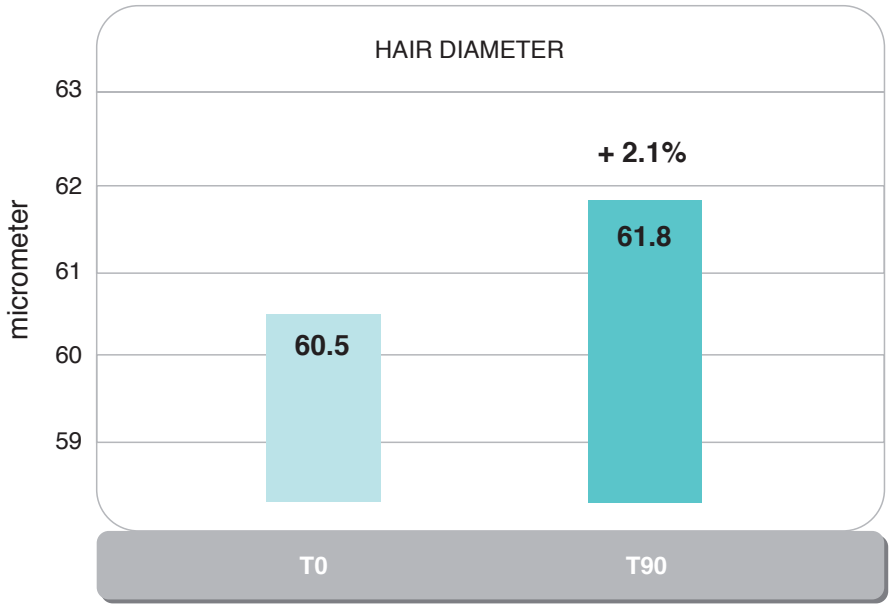
Efficacy Studies on Crescina

08-17 – JULY 2008

Crescina Re-Growth – *In vivo* test
Phototrichogram



Crescina Re-Growth – *In vivo* test



Efficacy Studies on Crescina

09-19 – JULY 2009

11. Evaluation of the efficacy and the cosmetic quality of an active lotion in facilitating physiological hair regrowth, under normal conditions of use and after 90 consecutive days of use.

The purpose of this test was to evaluate the cosmetic properties and effectiveness in helping the physiological regrowth of hair of a cosmetic product named Crescina Re-Growth.
The cosmetic effectiveness was evaluated using the technique of phototrichogram, carried out at the time of inclusion, and after 60 and 90 days of treatment. 20 subjects were included in the study – 10 males and 10 females, 14 subjects with medical histories of telogen effluvium and 6 subjects with medical histories of androgenic alopecia at grades II and III of the Hamilton-Norwood scale for men and at grades I and II of the Ludwig scale for women. Age: 20 to 55 years old

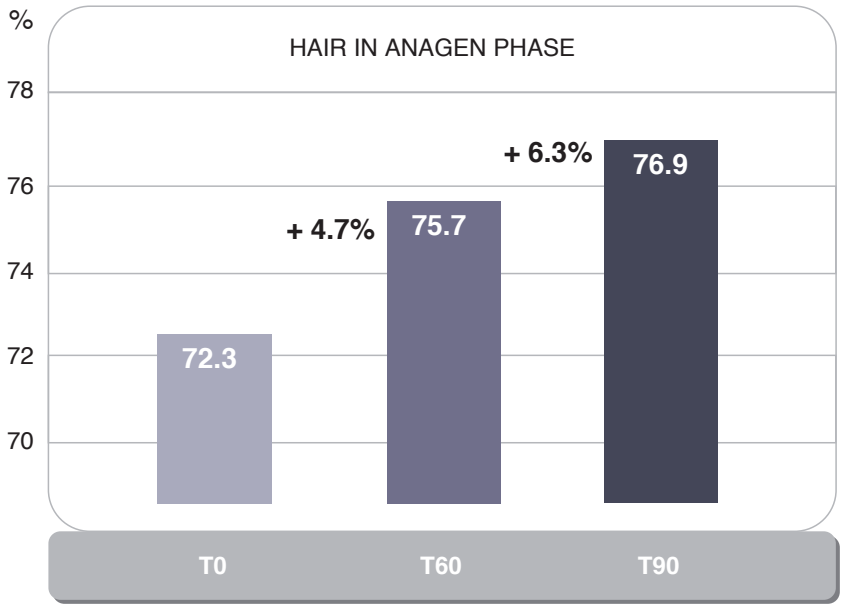
The results obtained after 90 days of treatment highlighted that the treatment under examination:
- generated an increase of 6.57% in the number of hair in the anagen phase
- generated a reduction of 15.61% in the number of hair in the telogen phase
- generated an increase of 6.31% in the percentage of hair in the anagen phase
- generated a reduction of 16.52% in the percentage of hair in the telogen phase

On the basis of the results obtained during the course of the study, we can state that Crescina Re-Growth demonstrated good cosmetic effectiveness in helping the physiological regrowth of hair.

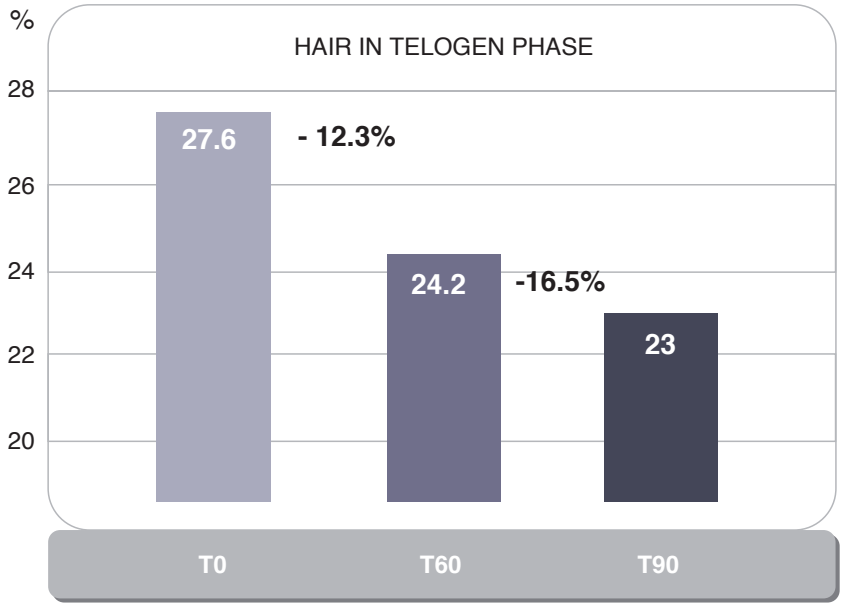
Efficacy Studies on Crescina

09-19 – JULY 2009

Crescina Re-Growth – *In vivo* test
Phototrichogram



Crescina Re-Growth – *In vivo* test
Phototrichogram



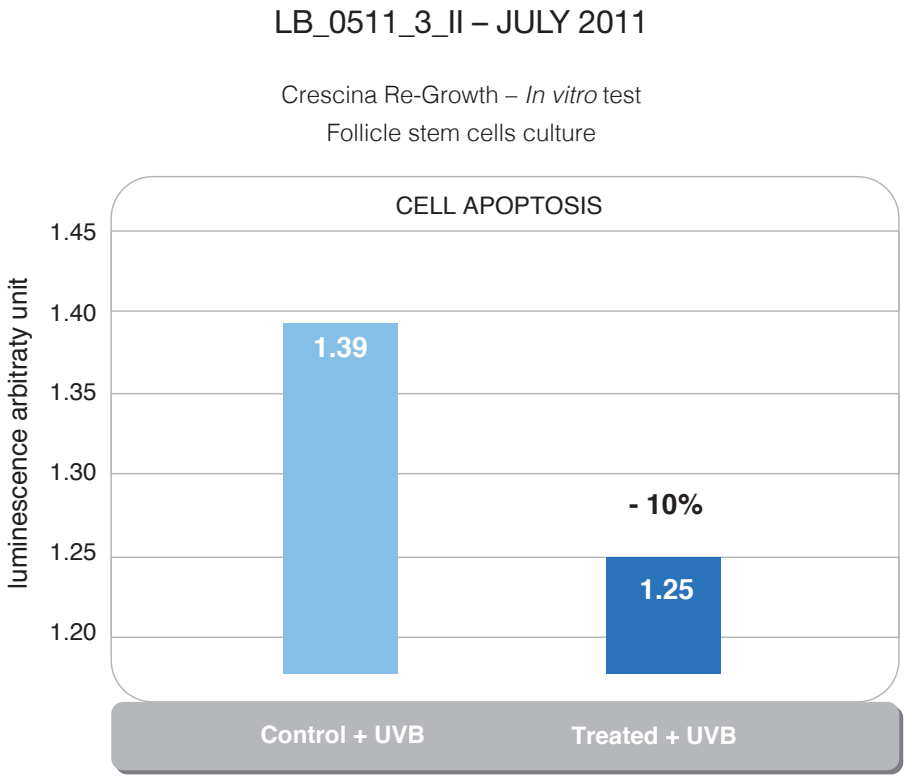
Efficacy Studies on Crescina

LB_0511_3_II – JULY 2011

12. *In vitro* study on hair follicle stem cells.

Cell culture of human Hair Follicle Stem Cells (HFSC) has been performed in order to test active compounds for the preservation of stem cells niches. Apoptosis quantification (Caspases 3/7 assay) to be performed 20 hours after UV irradiation.
Hydrolyzed Rice Protein (Stem-Engine in Crescina Re-Growth) has shown to induce a reduction of apoptosis of -10% (vs control) when tested at 0,05%. In order to perform a more refined dose-dependent analysis, the test of Hydrolyzed Rice Protein has been repeated at lower concentrations. Taking into account all the results, it can be hypothesize that Hydrolyzed Rice Protein exerts a protective action against DNA damage in Hair Follicle Stem Cells. The data may be of particular interest since the action have been exerted following only 24 hours of incubation.
The pictures of the cell cultures (not shown), following KI67/TUNEL/DAPI triple immunostaining, seem to confirm the obtained results, showing a lower presence of green positive (i.e. apoptotic) cells in percentage.

Efficacy Studies on Crescina



Efficacy Studies on Crescina

SELF-ASSESSMENT TEST – MARCH 2012

13. Efficacy study of Crescina Re-Growth.

Labo collects, for several years, the consumers' satisfaction results, about its product, Crescina Re-Growth, through a short pen&paper questionnaire, provided in pharmacies that sell the product. Overall, starting from 2001, 7.300 questionnaires have been given to Crescina consumers. Labo has requested to GN Research to analyze the results of these questionnaires to evaluate the performance achieved by Crescina over the time (from 2001 at present).
The questionnaires have been administrated to consumers of the Crescina Re-Growth product, random selected in pharmacy. The random selection rule to interview the consumers has allowed to obtain a reliable sample, and to achieve consistent results. Even if no quota (e.g. sex, age, etc.) has been established a priori, as the distribution of the Crescina consumers universe has not been known, the randomness with which the consumers have been found in pharmacy and the high number of cases analyzed (7.300) guarantee anyway the fact that the sample achieved reflects the real distribution of the Crescina consumers.

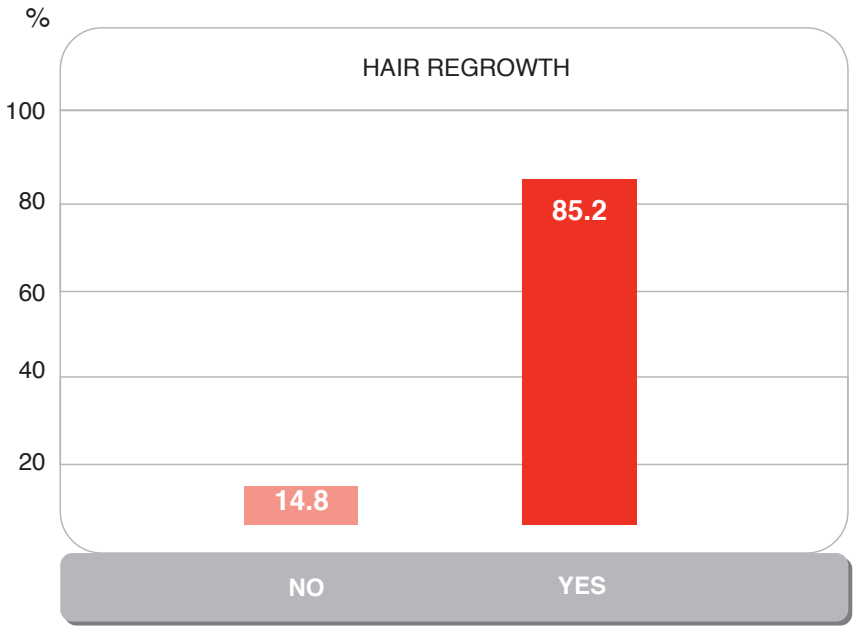
85% of the interviewed declares that, after using Crescina product, they have obtained results in terms of hair growth, in the parts affected by hair loss.

85% of the interviewed declares that, after using Crescina product, they have noticed an increase in the hair thickness

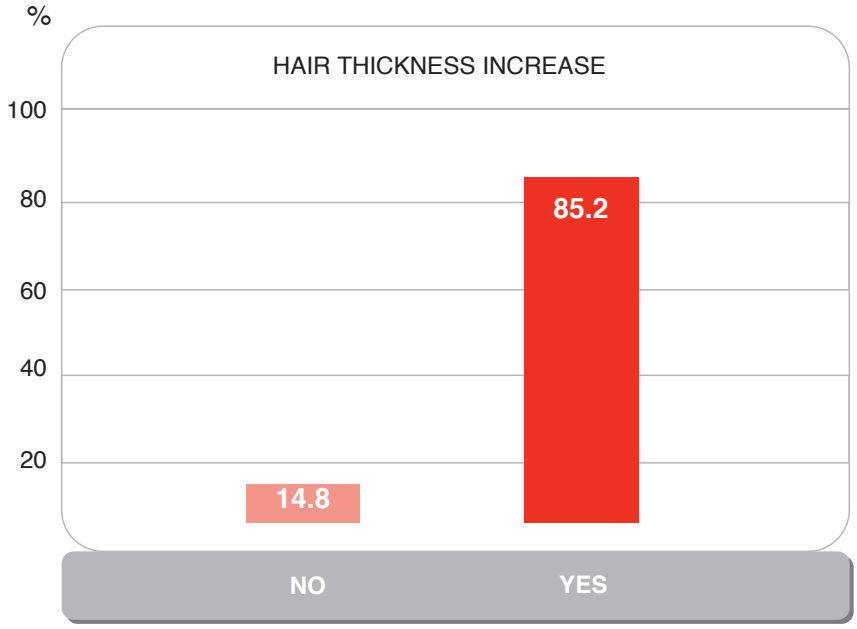
Efficacy Studies on Crescina

SELF-ASSESSMENT TEST – MARCH 2012

Crescina Re-Growth – Self evaluation
7.300 consumers



Crescina Re-Growth – Self evaluation
7.300 consumers



Efficacy Studies on Crescina

SELF-ASSESSMENT TEST – APRIL 2012

14. Efficacy study of Crescina Re-Growth HFSC.

Labo collects, since several years, the consumers' satisfaction results, about its product, Crescina Re-Growth, through a short pen & paper questionnaire, provided in pharmacies that sell the product. Labo has requested to GN Research to analyze the results of questionnaires evaluating the performance achieved by Crescina Re-Growth.

The questionnaires have been administrated to Crescina Re-Growth HFSC consumers, randomly selected in pharmacies. The random selection rule to interview the consumers has allowed to obtain a reliable sample, and to achieve consistent results. Even if no quota (e.g. gender, age, etc.) has been established a priori, as the distribution of the Crescina HFSC consumers universe is not known, the randomness with which the consumers have been found in pharmacy and the high number of cases analyzed (230) guarantee anyway the fact that the sample achieved reflects the real distribution of the Crescina HFSC consumers.

For each question, in addition to the percentage distribution of the answers, a significance test has been done, to evaluate if it is possible to exclude all the elements of randomness in the results achieved (and consequently if the difference in the answers can be considered statistically significant).

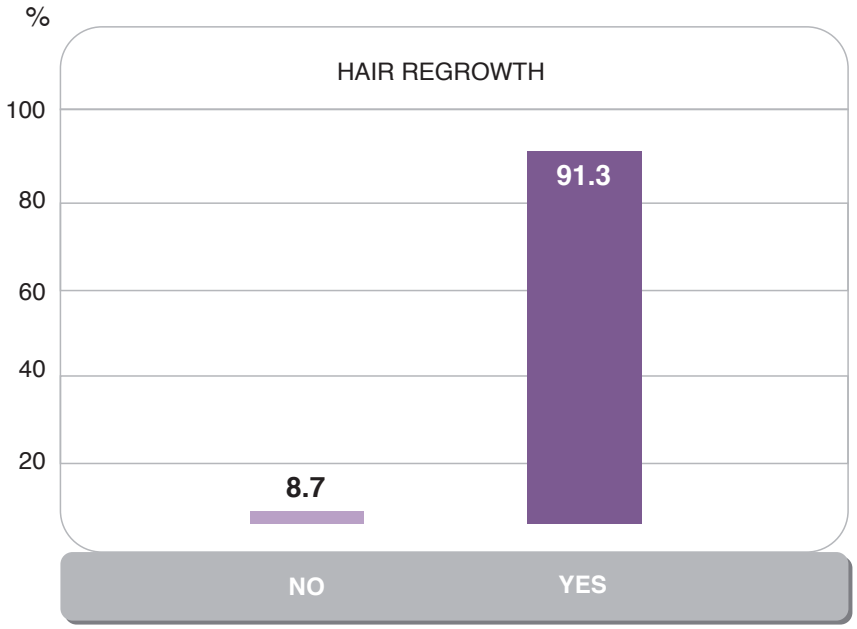
91,3% of the interviewed declares that, after having used Crescina HFSC product, they have obtained results in terms of hair growth, in the parts affected by hair loss. 88,7% of the sample declares that, after using Crescina HFSC product, has noticed an increase in the hair thickness.

Almost all the consumers declare to be satisfied with the product, considered of a good quality, consistent with the expectations and effective.

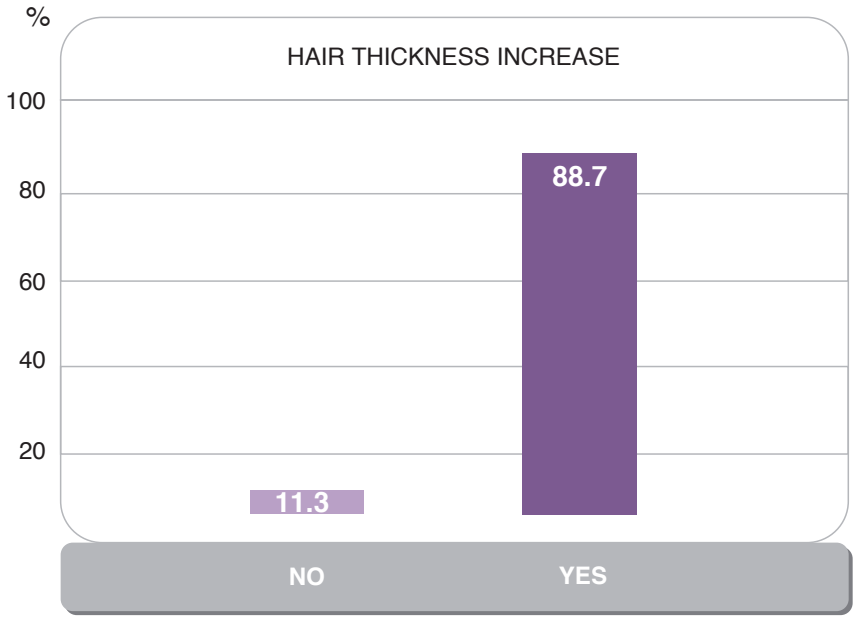
Efficacy Studies on Crescina

SELF-ASSESSMENT TEST – APRIL 2012

Crescina Re-Growth HFSC – Self evaluation
230 consumers



Crescina Re-Growth HFSC – Self evaluation
230 consumers



Efficacy Studies on Crescina

F.U.05.C.L._2011/2192 – APRIL 2012

15. Clinical-instrumental, double blind, randomised, placebo-controlled study on the efficacy of a cosmetic lotion, Crescina Re-Growth HFSC, to aid hair growth in thinning and bald areas.

The study hereby described is aimed to evaluate the efficacy of a cosmetic lotion, Crescina Re-Growth HFSC, supporting the treatment of the male androgenetic alopecia. On this purpose, controlled clinical-instrumental study is carried out on 46 (23 subjects for each treatment arm) healthy men showing the clinical signs of androgenentic alopecia type from II to IV. After 2 and 4 months, product efficacy is evaluated by phototrichogram and pull test technique.
The study is carried out as follows: a) in double blind conditions, b) placebo controlled, c) randomized.
Based on the results obtained in this study it is possible to assess that - in subjects having alopecia type II,III and IV – Crescina Re-Growth HFSC demonstrated a good cosmetic efficacy supporting the physiological hair growth. Compared to baseline evaluation (T0) after two months of treatment the phototrichogram showed, in the 95.7% of the subjects, an increase of hair in re-growth phase (anagen) by 11.5% and a decrease of hair in rest phase (telogen) by – 18.6%. Furthermore, in the 89.5% of the subjects tested, the capacity of hair to remain attached to its bulb after traction (resistance to traction – pull test) increased by 29.9% (not shown).
Compared to baseline evaluation T0, after 4 months of treatment the phototrichogram showed, in the 100% of the subjects, an increase of hair in re-growth phase (anagen) by 18.2% and a decrease of hair in rest phase (telogen) by 29.1%. Furthermore, in the 100 % of the subjects tested, the capacity of hair to remain attached to its bulb after traction (resistance to traction – pull test) increased by 46.8% (not shown).
The variations reported for the active product are statistically significant at all the experimental times monitored. The variations of the parameters analysed for the active product are all higher than the placebo product, in all the experimental times monitored.

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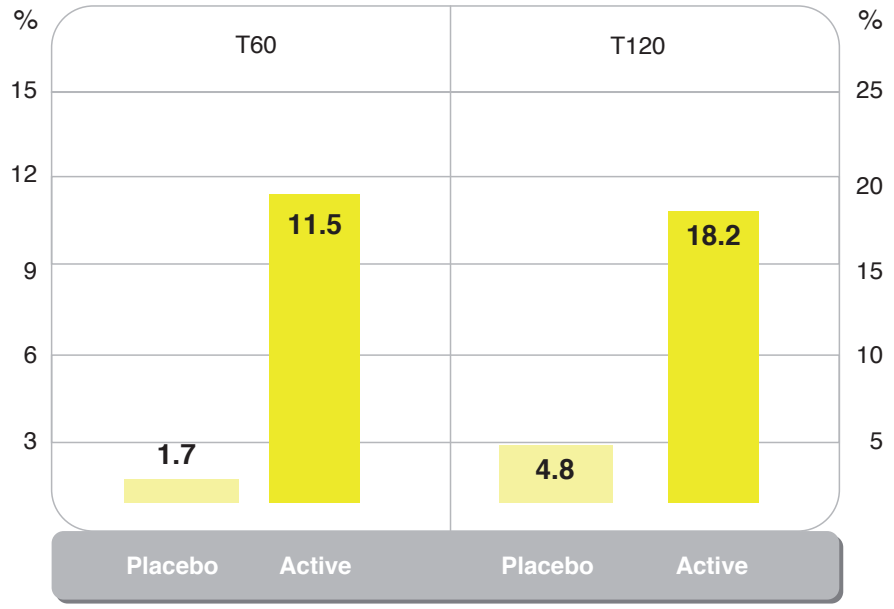
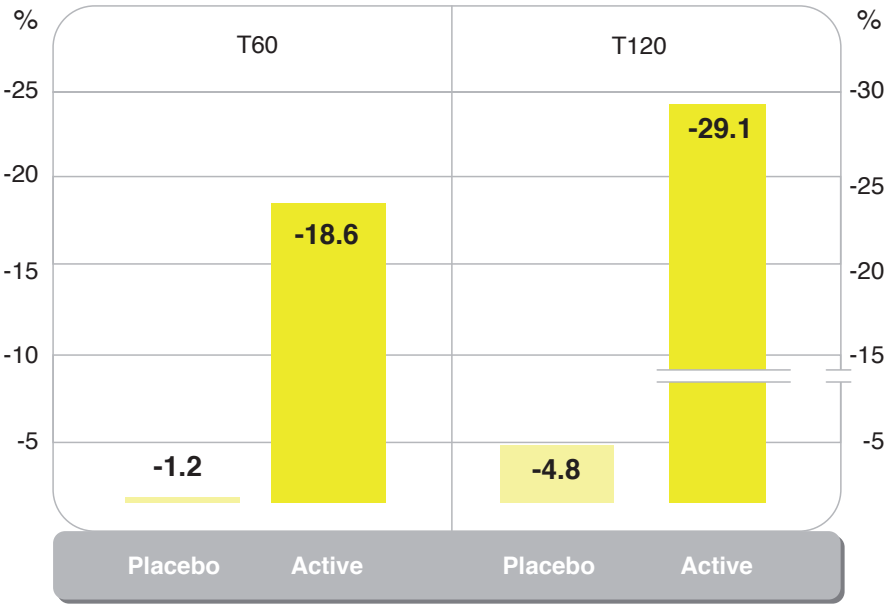
Efficacy Studies on Crescina

F.U.05.C.L._2011/2192 – APRIL 2012

Crescina Re-Growth HFSC – *In vivo* test
Phototrichogram – Anagen variation vs T0



Crescina Re-Growth HFSC – *In vivo* test
Phototrichogram – Telogen variation vs T0



Efficacy Studies on Crescina

TV.01.C_2014/3129 – MARCH 2015

16. *Ex vivo* evaluation of the absorption potential of the aminoacids, vitamins, oligoelements and nucleic acids contained in a mix through the skin (epidermis + dermis).

The aim of the this study was to investigate the capability of different molecules with different chemical and biological features (aminoacids, vitamins, oligoelements and nucleic acids) to be absorbed through the skin, quantifying the amount available in epidermis and in dermis.
The experimental system is the Franz Diffusion Cell, on which the treated skin was anchored; the skin portions used in this test were: epidermis and epidermis + dermis.
The Franz Cell chamber is an in vitro apparatus for skin permeation assay. The Franz Cell apparatus consists of two primary chambers separated by a membrane. The test product is applied to the membrane via the donor chamber. The receptor chamber contains fluid from which samples are taken for analysis. The chamber is maintained at a constant temperature (test temperatures different by the room one are obtained by liquid flow in the temperature control jacket.
In the monitored experimental period, molecule absorption is significant and time-dependent.
After 24 hours from application, Glycine highlight a time-dependent total absorption of 75,9%.

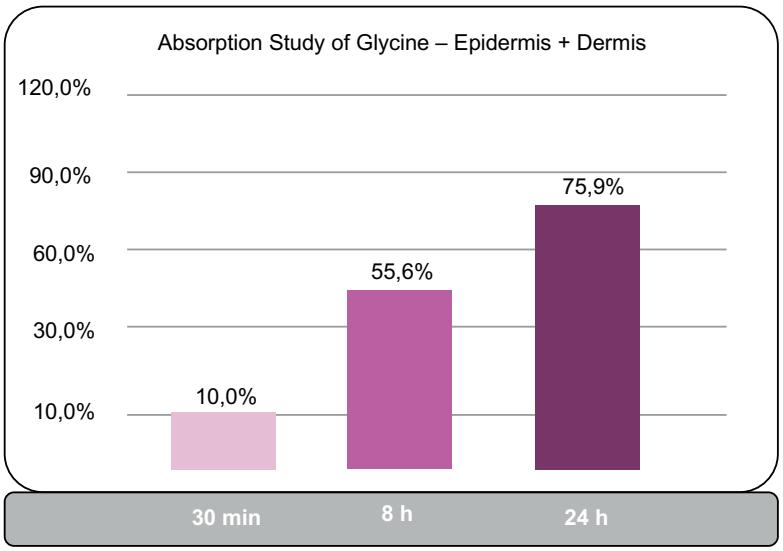
MOLECULE	MOLECULAR WEIGHT (IN DALTON)
GLYCINE	75,07

LABO COSPROPHAR

SWISS PATENT CH 703 390

Efficacy Studies on Crescina

TV.01.C_2014/3129 – MARCH 2015



Efficacy Studies on Crescina

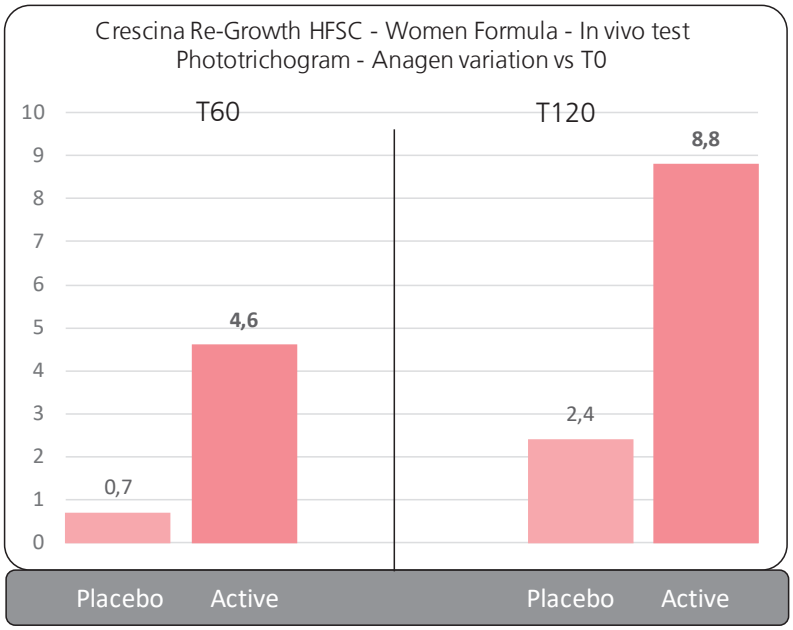
1405 G16F – APRIL 2015

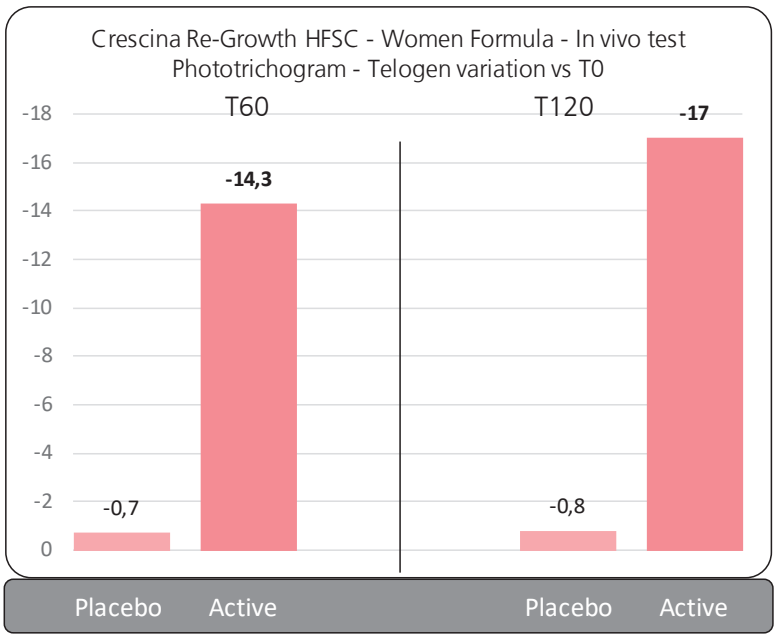
17. Evaluation of the efficacy and tolerability of a hair cosmetic treatment helping hair growth in the thinning areas, through clinical-instrumental test, double-blind and placebo controlled (Women). 1405 G16F – April 2015.

Scope of this clinical test is to evaluate the efficacy of a hair cosmetic treatment mainly in helping hair growth in women. The clinical-instrumental study is double-blind and placebo controlled. Furthermore, skin and scalp tolerability of the product has been evaluated too.
The clinical test was coordinated by a medical dermo-cosmetological center and performed also at a dermatologist medical studio.
42 female volunteers, aged between 20 and 60 years and with localized or spread hair thinning (grades from I-1 to I-4 Ludwig Scale), were recruited. Volunteers have been divided into two groups of 21 persons each: the first group applied the active product (i.e. Crescina HFSC), whereas the second group used the
placebo (the active ingredients have been omitted in the formulation of the placebo) for 5 consecutive days followed by 2 days of stop, for a 120-day period. During this period, any change affecting the skin and the scalp has been recorded and specific instrumental, anthropometric and clinical parameters have been evaluated. Notably, after 120 days of product use, compared to T0, the phototrichogram highlighted the following variations: 8.8% average improvement of hair in anagen for the active group vs 2.4% for the placebo group; -17% average reduction of hair in telogen for the active group vs -0.8 for the placebo group.

Efficacy Studies on Crescina

1405 G16F – APRIL 2015





Efficacy Studies on Crescina

TV.01.C_2015/1914 – OCTOBER 2015

18. *In vitro* evaluation of the absorption potential of the following cosmetic active molecules through the skin (epidermis + dermis).

The aim of the this study was to investigate the capability of molecules with different chemical and biological features to penetrate through the skin, quantifying the amount available in epidermis and in dermis.
The experimental system is the Franz Diffusion Cell, on which the treated skin was anchored; the skin portions used in this test were: epidermis and epidermis + dermis.
The Franz Cell chamber is an in vitro apparatus for skin permeation assay. The Franz Cell apparatus consists of two primary chambers separated by a membrane. The test product is applied to the membrane via the donor chamber. The receptor chamber contains fluid from which samples are taken for analysis. The chamber is maintained at a constant temperature (test temperatures different by the room one are obtained by liquid flow in the temperature control jacket.
In the monitored experimental period, molecule absorption is significant and time-dependent.
After 24 hours from application, Copper Tripeptide-1 highlight a time-dependent total absorption of 77,0%.

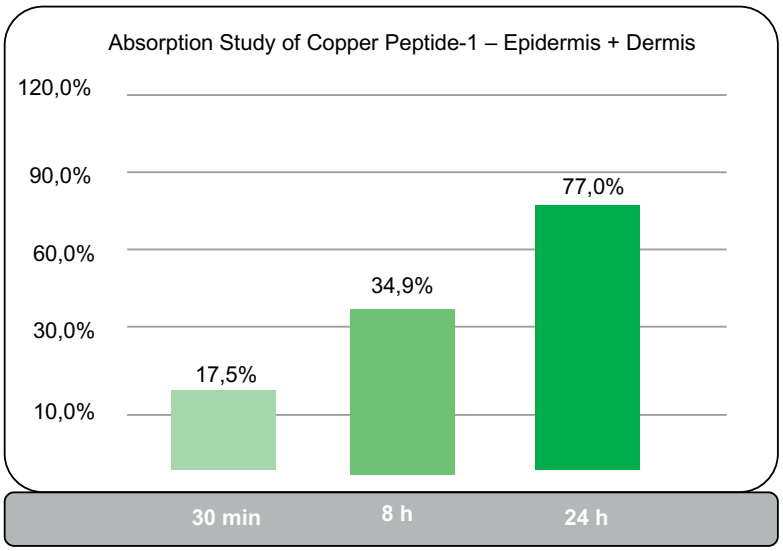
MOLECULE	MOLECULAR WEIGHT (IN DALTON)
COPPER TRIPEPTIDE-1	404,00

LABO
LABO COSPROPHAR

SWISS
PATENT
CH 703 390

Efficacy Studies on Crescina

TV.01.C_2015/1914 – OCTOBER 2015



Efficacy Studies on Crescina

TV.01.C_2015/3266 – MARCH 2016

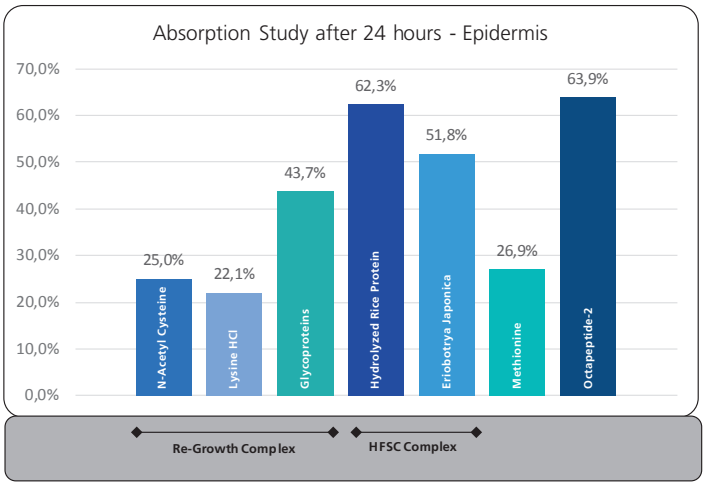
19. *In vitro* evaluation of the absorption potential of the following cosmetic active molecules (N-Acetyl Cysteine, Lysine HCl, Glycoproteins, Methionine, Octapeptide-2, Hydrolyzed Rice Protein, Eriobotrya Japonica Leaf Extract) through the skin (Epidermis+Dermis) in presence of an enhancer mixture composed by 3 cosmetic helpers. TV.01.C_2015/3266. March 2016.

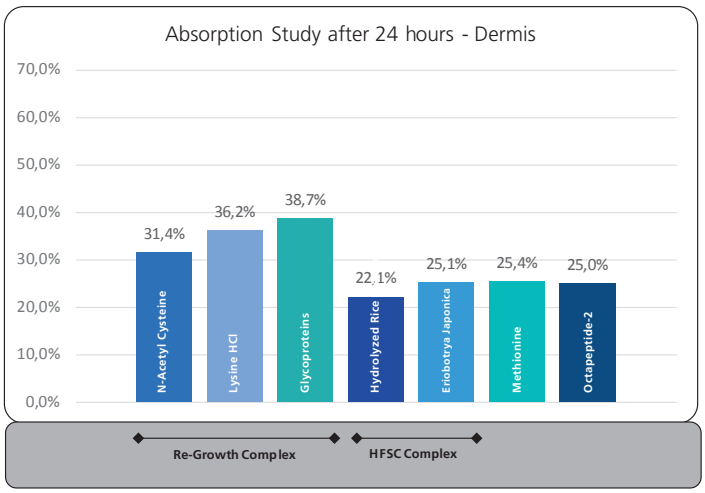
The aim of this study was to investigate the capability of molecules with different chemical and biological features to penetrate through the skin in presence of a mixture of cosmetic raw materials with enhancer activity (Pentylene Glycol, Caprylyl Glycol, Decylene Glycol), quantifying the amount available in epidermis and dermis.
The absorption system was the Franz Diffusion Cell. The Franz Diffusion Cell is an *in vitro* apparatus for skin permeation assay. The Franz Cell apparatus consists of two primary chambers separated by a membrane. The test product is applied to the membrane via the donor chamber. The receptor chamber contains fluid from which samples are taken for analysis. The chamber is maintained at a constant temperature (test temperatures different from the room ones are obtained by liquid flowing in the temperature control jacket).
Solutions of the active molecules were applied on the tissues and the membranes analyzed after 30 minutes, 8 hours and 24 hours.
By means of the molecule concentrations obtained by the analytical dosages, the quantity of each molecule penetrated through the skin structures (epidermis and epidermis+dermis) was calculated and expressed as penetration percentage in comparison with the applied quantity.

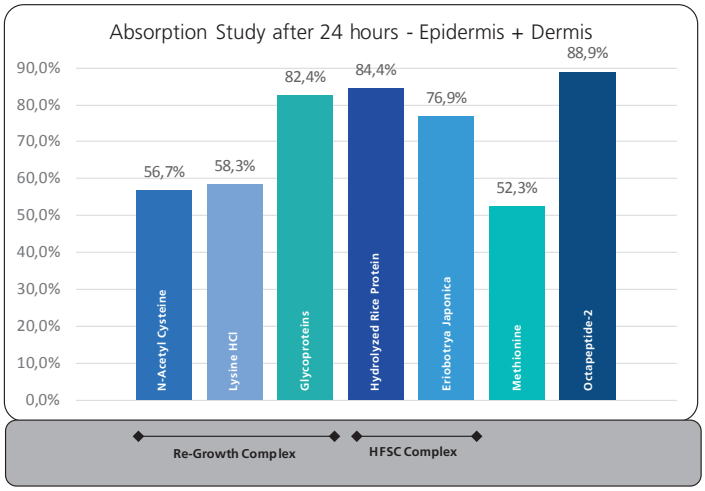
MOLECULE	MOLECULAR WEIGHT (IN DALTON)
N-ACETYL CYSTEINE	163.2
LYSINE HCL	146.2
GLYCOPROTEINS	20,000
HYDROLYZED RICE PROTEIN	3,500
ERIOBOTRYA JAPONICA	472.7
METHIONINE	149.2
OCTAPEPTIDE-2	1,017.2

Efficacy Studies on Crescina

TV.01.C_2015/3266 – MARCH 2016







Clinical Efficacy of a Cosmetic Treatment by

Crescina® Human Follicle Stem Cell on Healthy Males with Androgenetic Alopecia

SWISS PATENT
CH 703 390

Clinical Efficacy of a Cosmetic Treatment by Crescina® Human Follicle Stem Cell on Healthy Males with Androgenetic Alopecia

Clinical Efficacy of a Cosmetic Treatment by Crescina® Human Follicle Stem Cell on Healthy Males with Androgenetic Alopecia

Dermatol Ther (Heidelb)
DOI 10.1007/s13555-013-0021-2

ORIGINAL RESEARCH

Clinical Efficacy of a Cosmetic Treatment by Crescina® Human Follicle Stem Cell on Healthy Males with Androgenetic Alopecia

Daniela Buonocore · Vincenzo Nobile · Angela Michelotti · Fulvio Marzatico

To view enhanced content go to www.dermtherapy-open.com
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ABSTRACT

Introduction: Androgenetic alopecia (AGA) is the most common cause of hair loss among males, characterized by progressive thinning of the scalp hairs and defined by various patterns. The main factors underling hair loss in AGA are genetic predisposition and increased sensitivity of the hair follicles to androgens, leading to a shortening of the anagen phase. In the present study, the authors investigated the efficacy of a commercially available cosmetic lotion, Crescina® HFSC (human follicle stem cell; Labo Cosprophar AG, Basel, Switzerland), in promoting hair growth and in decreasing hair loss.

Methods: A placebo-controlled, randomized trial was carried out on healthy males suffering from alopecia grade II to IV. Anagen rate and hair resistance to traction (pull test) were assessed after 2 and 4 months of treatment using phototricogram and pull test technique.

Results: Crescina® HFSC applied for 4 months was effective in promoting hair growth and in decreasing hair loss. After 2 and 4 months of treatment, the anagen rate was increased by 6.8% and 10.7%, respectively. Hair resistance to traction was decreased by 29.6% and 46.8%, respectively.

Conclusions: The present study demonstrated the positive effect of Crescina® HFSC in modulating the activity of the hair follicle and promoting hair growth.

Keywords: Anagen rate; Androgenetic alopecia; Cosmetics; Crescina® HFSC; Hair growth; Hair loss; Pull test; Topical application

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INTRODUCTION

Androgenetic alopecia (AGA) is the most common cause of hair loss among males [1].

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Clinical Efficacy of a Cosmetic Treatment by Crescina® Human Follicle Stem Cell on Healthy Males with Androgenetic Alopecia

It is characterized by progressive thinning of the scalp hairs, defined by various patterns [2], which can start at any age after puberty and is potentially reversible. Even if from a medical point of view, AGA is considered a relatively mild condition; however, people suffering from this condition consider AGA a serious condition that impacts their self-esteem, well-being, social relationships, and confidence.

The main factors underling hair loss in AGA are genetic predisposition and increased sensitivity of the hair follicles to androgens [3]. AGA is often precipitated and exacerbated by conditions that can induce telogen effluvium, including drugs, acute stressors, and weight loss [4]. However, in recent years it has been shown that other factors, such as microinflammation [5], decreased microcirculation [6], and aging [7], can cause hair loss in AGA. These changes contribute to shifting the normal balance of the hair cycle leading to a shortening of the anagen phase. The major components of balding in AGA are frontotemporal recession and loss of hair over the vertex. Hairs become shorter and finer, and finally complete hair loss occurs except at the lateral and posterior margins of scalp, where hair is retained.

Histologically, in AGA large terminal follicles diminish in size during hair cycles, and the resulting miniaturized follicle eventually produces a microscopic hair. Testosterone is necessary for miniaturization, and 5-alpha-reductase inhibitors, which block the conversion of testosterone to its more active form dihydrotestosterone (DHT), delay the progression of AGA [8]. Recently, Garza and coworkers [9] reported the preservation of stem cell population and a decreased conversion of hair follicle stem cells to progenitor cells in bald scalp biopsies from AGA individuals. This finding is consistent with the current clinical concept that AGA is a nonscarring type of alopecia and suggests potential reversibility of the condition.

Currently, only two medications, based on finasteride and minoxidil as active pharmacological ingredients, are approved by the US Food and Drug Administration (FDA) for AGA treatment. However, they are costly, require lifelong treatment, and may have side effects. Furthermore, people are frequently reluctant/intimidated by the pharmacological approach to treat a disease that is not life threatening. Thus, a topical, nonpharmacological, effective cosmetic treatment could be more acceptable to patients.

The aim of the present study was to assess the efficacy of the use of a patented (US 6,479,059 B2 and CH 703 390), topical cosmetic product, Crescina® HFSC (human follicle stem cell; Labo Cosprophar AG, Basel, Switzerland), claimed to be effective for the treatment of male AGA [10]. The active ingredients contained in the product were chosen to obtain three main effects: proliferation of the stem cells of both the bulge and the dermal papilla, keratinization, and stimulation of microcirculation. Stem cell and dermal papilla stem cell proliferation was achieved by hydrolyzed rice protein and corosolic acid, respectively. Keratinization was stimulated by cysteine, lysine, and a glycoprotein (lectin). Microcirculation was stimulated by benzyl nicotinate. The mentioned results were obtained from studies commissioned by the company Labo Cosprophar AG, which has filed a patent (CH 703 390 B1) [10].

Clinical Efficacy of a Cosmetic Treatment by Crescina® Human Follicle Stem Cell on Healthy Males with Androgenetic Alopecia

Dermatol Ther (Heidelb)

MATERIALS AND METHODS

All the study procedures were carried out according to World Medical Association's (WMA) Helsinki Declaration and its amendments (Ethical Principles for Medical Research Involving Human Subjects, adopted by the 18th WMA General Assembly Helsinki, Finland, June 1964 and amendments). To participate in the study, each participant was fully informed on study risks and benefits, aims, and procedures. An informed consent form and a consent release for publication of photos were signed by the subject prior to participating in the study.

Subjects and Study Design

Healthy male volunteers suffering from alopecia grade II to IV according to the Hamilton–Norwood scale [11] (Fig. 1) were enrolled in the study. Subjects were enrolled in the study by a certified dermatologist if they fulfilled the inclusion and exclusion criteria laid down in the study design (Table 1) were applicable. Clinical examination was carried out in order to evaluate the degree and pattern of hair loss, and hair (length, diameter, and breakage) and scalp (inflammation, erythema and, scaling) conditions. Active and placebo treatments were then allocated by means of the Efron's biased coin algorithm using PASS 11 (version 11.0.8 for Windows; PASS, LLC., Kaysville, UT, USA). The tested and the placebo products were used for 4 months according to the following procedure: apply one vial (5 mL) of the product on clean and dry scalp, line by line, concentrating on the areas where thinning is more evident; massage gently to aid penetration; apply every day for 5 consecutive days, stop the treatment for 2 days and then continue the application.

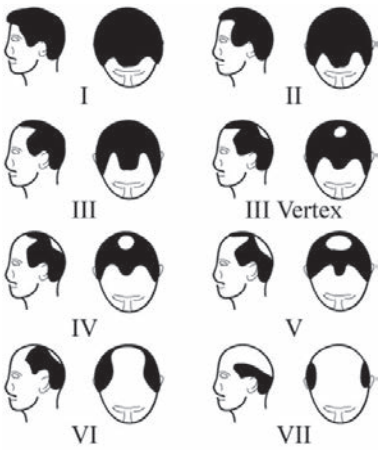

Fig. 1 Hamilton–Norwood classification

Tested Product

The tested product is a commercially available cosmetic lotion named Crescina® HFSC. The ingredients of the tested product and placebo are listed in Table 2.

Phototricogram

A transitional area of hair loss between normal hair and the balding area of 1.8 cm^2 was defined using a stencil template and chosen for clipping. The clipped hairs within the target area were dyed for gray or fair hairs with a commercially available solution (RefectoCil®, GW Cosmetics GmbH, Leopoldsdorf, Germany) in order to enhance their contrast. Thereafter, the dyed hairs were cleansed using an alcoholic solution and digital images were taken while the area was still wet with a digital close-up camera. Images were taken at day 0, immediately after clipping, and 2 days after

Clinical Efficacy of a Cosmetic Treatment by Crescina® Human Follicle Stem Cell on Healthy Males with Androgenetic Alopecia

Table 1 Inclusion and exclusion criteria

Inclusion criteria
Healthy male subjects
Age between 20–55 years old
Type: Caucasian race
Subjects showing clinical signs of androgenetic alopecia type II–IV
Subjects who have not used antihair loss treatments the 6 months before the study start
Promise to not use topical and/or systemic products with similar effect to that one of the product to be tested throughout the study period
Promise to not change the daily routine
Exclusion criteria
Subjects who do not fit the inclusion criteria
Subjects with allergies or sensitivity to cosmetic products, toiletries, sunscreens and/or topical drugs
Disorder of the scalp
Subjects with dermatological problems on the test area
Subjects under pharmacological treatment (both locally or systemically)
Positive anamnesis for atopy

Table 2 Ingredient INCI listings of formulations investigated

Formulation A: test active ingredients	Formulation B: placebo control
Alcohol denat., aqua, glycerin, butylene glycol, lysine hydrochloride, benzyl nicotinate, acetyl cysteine, benzophenone-4, disodium EDTA, glycyrrhetinic acid, menthol, sodium hydroxide, silanediol salicylate, triethanolamine, serine, threonine, propylene glycol, adenosine, allantoin, zinc acetylmethionate, hematite extract, hydrolyzed rice protein, phosphatidylcholine, hydrolyzed soy protein, hydrolyzed DNA, hydrolyzed MA, *Eriobotrya japonica* leaf extract, salicylic acid, glycogen, glycoproteins, *Artemia* extract, C.I. 14720, C.I. 16255, C.I. 19140, C.I. 28440, C.I. 73015	Alcohol denat., aqua, disodium EDTA, sodium hydroxide, C.I. 14720, C.I. 16255, C.I. 19140, C.I. 28440

EDTA ethylenediaminetetraacetic acid, *INCI* International Nomenclature of Cosmetic Ingredients

clipping. These two photographs were then examined by a software system that is able to recognize individual hair fibers in the photographs. By comparing the two photographs, the computer can determine which hairs are growing (anagen hairs) and

Clinical Efficacy of a Cosmetic Treatment by Crescina® Human Follicle Stem Cell on Healthy Males with Androgenetic Alopecia

Dermatol Ther (Heidelb)

which are not (telogen hairs). The same procedure was carried out after 2 and 4 months of treatment.

Pull Test

Gentle traction was exerted on a cluster of hairs (approximately 60 hairs) on at least three different areas of the scalp, and the number of extracted hairs was counted. Normally, less than three telogen-phase hairs should come out with each pull [12]. If at least three hairs were obtained with each pull or if more than ten hairs total were obtained, the pull test was considered positive and suggestive of telogen effluvium.

Global Photographic Assessment

Patients were asked to maintain the same hair style, color, and length throughout the study. Standardized global photographs of the frontal/parietal region were taken using a digital camera equipped with a macro lens.

Statistical Analysis

An intention to treat statistical analysis was performed using NCSS 8 (version 8.0.4 for Windows; NCCS, LLC., Kaysville, UT, USA). Data were checked for normality using either the Shapiro–Wilk W, Kolmogorov–Smirnov, and D'Agostino omnibus normality tests. If the data were normal, the repeated measure analysis of variance (RM-ANOVA) followed by Tukey–Kramer multiple comparison test was performed both for intra- and inter-group comparisons. If data were not normal, the Wilcoxon signed-rank test was performed for intra-group comparisons, whereas the Mann–Whitney *U* test was performed for inter-group comparisons. Values are expressed as arithmetic mean ± standard deviation (SD). $P < 0.05$ was considered significant.

RESULTS

Forty-six healthy male volunteers (Table 3) suffering from alopecia grade II to IV were enrolled in the study.

Anagen

The results of anagen hair rates (as %) at baseline (T0), 2 (T2), and 4 (T4) months are reported in Table 4 and Fig. 2. Baseline mean anagen hair rate was similar between active (63.8 ± 4.2%) and placebo (62.8 ± 4.3%) groups, and not statistically significant ($P > 0.05$). At the 2 months follow-up, only the active product group demonstrated a statistically significant improvement of anagen hair rate (70.6 ± 6.9%); while in the placebo (63.7 ± 5.0%) group no changes were observed. At 4 months, the active product group showed an additional statistically significant increment of the mean anagen rate (74.5 ± 5.6%). A slight statistical improvement

Table 3 Baseline characteristics of the randomized subjects

	Crescina® HFSC ($n = 23$)	Placebo ($n = 23$)
Mean age ± SD, years	34.7 ± 11.2	
Mean baseline anagen ratio ± SD	63.8 ± 4.2%	62.8 ± 4.3%
Hamilton–Norwood score, no. (%) of individuals		
Type II	5 (21.7)	5 (21.7)
Type III	10 (43.5)	11 (47.8)
Type III vertex	5 (21.7)	4 (17.4)
Type IV	3 (13.0)	3 (13.0)

HFSC human follicle stem cell, *SD* standard deviation

Clinical Efficacy of a Cosmetic Treatment by Crescina® Human Follicle Stem Cell on Healthy Males with Androgenetic Alopecia

Table 4 Results of anagen hair count (%)

	Active product					Placebo product				
	n	Mean (±SD)	1st quartile	Median	3rd quartile	*n*	Mean (±SD)	1st quartile	Median	3rd quartile
T = 0 months	23	63.8 ± 4.2	62.4	64.3	67.4	23	62.8 ± 4.3	59.4	62.2	66.7
T = 2 months	23	70.6 ± 6.9	65.8	69.1	76.9	23	63.7 ± 5.0	59.9	62.5	65.9
T = 4 months	23	74.5 ± 5.6	69.8	73.9	77.7	23	65.0 ± 5.2	60.8	64.5	69.4

SD standard deviation

was also seen in the placebo group (65.0 ± 5.2%). The variation versus T0 (Fig. 3) of the anagen hair rate in the active product group was +6.8 and +10.7% after 2 and 4 months, respectively; whereas an improvement of +2.2% was seen in the placebo group only at 4 months. Statistical analysis of the mean anagen rate in the active group showed a time-dependent statistically significant improvement ($P < 0.001$); whereas in the placebo group, time was a source of variation only at 4 months ($P = 0.004$). Analysis of the mean anagen rate between the active group compared to the placebo group was also statistically significant ($P < 0.001$). The improvement of anagen rate in the active group was observed in 95.7% (at T2) and 100% (at T4) of the subjects participating in the trial; whereas in the placebo group it was seen in 56.5% (at T2) and 69.6% (at T4).

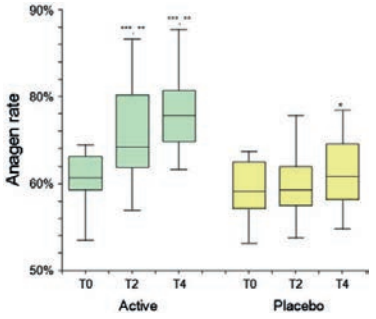

Fig. 2 Anagen rate (%) variation during the treatment. *$P < 0.05$ versus T0, **$P < 0.001$ active treatment versus placebo, ***$P < 0.001$ versus T0. *T0* baseline, *T2* 2 months, *T4* 4 months

Pull Test

The results of pull testing at baseline, 2, and 4 months are reported in Table 5 and Fig. 4. Baseline mean pulled hairs in the pull test was similar between the active (9.2 ± 1.3) and placebo (9.1 ± 1.8) groups, which was not statistically significant ($P > 0.05$). At the 2 months follow-up, only the active product group demonstrated a statistically significant improvement of 29.6% of hair resistance to traction (6.4 ± 1.8); whereas in the placebo (8.3 ± 2.1) group no changes were observed. At 4 months, the active product group

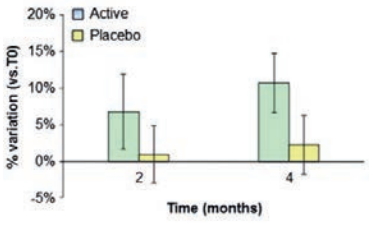

Fig. 3 Improvement of anagen rate (%) after the treatment. Data are reported as mean ± SD. *SD* standard deviation, *T0* baseline

Clinical Efficacy of a Cosmetic Treatment by Crescina® Human Follicle Stem Cell on Healthy Males with Androgenetic Alopecia

Dermatol Ther (Heidelb)

Table 5 Results of pull testing

	Active product					Placebo product				
	n	Mean (±SD)	1st quartile	Median	3rd quartile	*n*	Mean (±SD)	1st quartile	Median	3rd quartile
T = 0 months	19	9.2 ± 1.3	8	9	10	18	9.1 ± 1.8	8	9	10
T = 2 months	19	6.4 ± 1.8	5	6	8	18	8.3 ± 2.1	7	8	10
T = 4 months	19	4.8 ± 1.5	4	5	6	18	7.6 ± 1.9	6	8	9

SD standard deviation

showed an additional statistically significant increment of 46.8% of hair resistance (4.8 ± 1.5). A slight statistical improvement of 16.6% was also seen in the placebo group (7.6 ± 1.9). Statistical analysis of the mean anagen rate in the active group showed a time-dependent statistically significant improvement ($P < 0.001$); whereas in the placebo group, time was a source of variation only at 4 months ($P = 0.044$). Analysis of the hair fall in the hair pull test between the active group compared to the placebo group was also statistically significant ($P < 0.01$ and $P < 0.001$ at T2 and T4, respectively). The improvement of hair resistance to traction in the active group was observed in 89.5% (at T2) and 100% (at T4) of the subjects participating in the trial; whereas in the placebo group it was seen in 52.6% (at T2) and 78.9% (at T4).

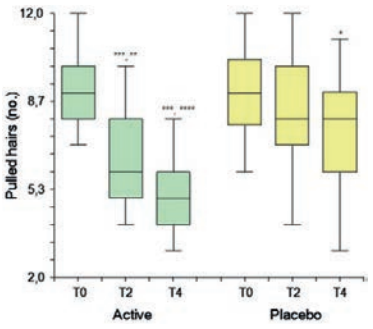

Fig. 4 Resistance to traction (pull testing) variation during the treatment. *$P < 0.05$ versus T0, **$P < 0.01$ active treatment versus placebo, ***$P < 0.001$ versus T0, ****$P < 0.001$ active treatment versus placebo. *T0* baseline, *T2* 2 months, *T4* 4 months

Global Photographic Assessment

Figure 5 shows the macroscopic effect of the product on hair growth. An increase in hair growth was seen in the frontal and parietal area (vertex) of the scalp.

DISCUSSION

Androgenetic alopecia is the most common cause of hair loss among males and has a psychosociologic impact on the well-being of the subject [1]. The pharmacologic treatment of AGA is expensive, requires lifelong treatment, and may have side effects. Subjects are also reluctant/intimidated to use drugs for a nonpathologic condition; however, use of cosmetics is more acceptable.

A large number of cosmetics claiming to be effective in the coadjuvant treatment of AGA are sold on the market, but some lack proof of effect, relying only on the effects of the raw materials. Contrary to this approach, new cosmetic regulations [13] require manufactures to demonstrate product efficacy in order to protect subjects from misleading claims.

Clinical Efficacy of a Cosmetic Treatment by Crescina® Human Follicle Stem Cell on Healthy Males with Androgenetic Alopecia

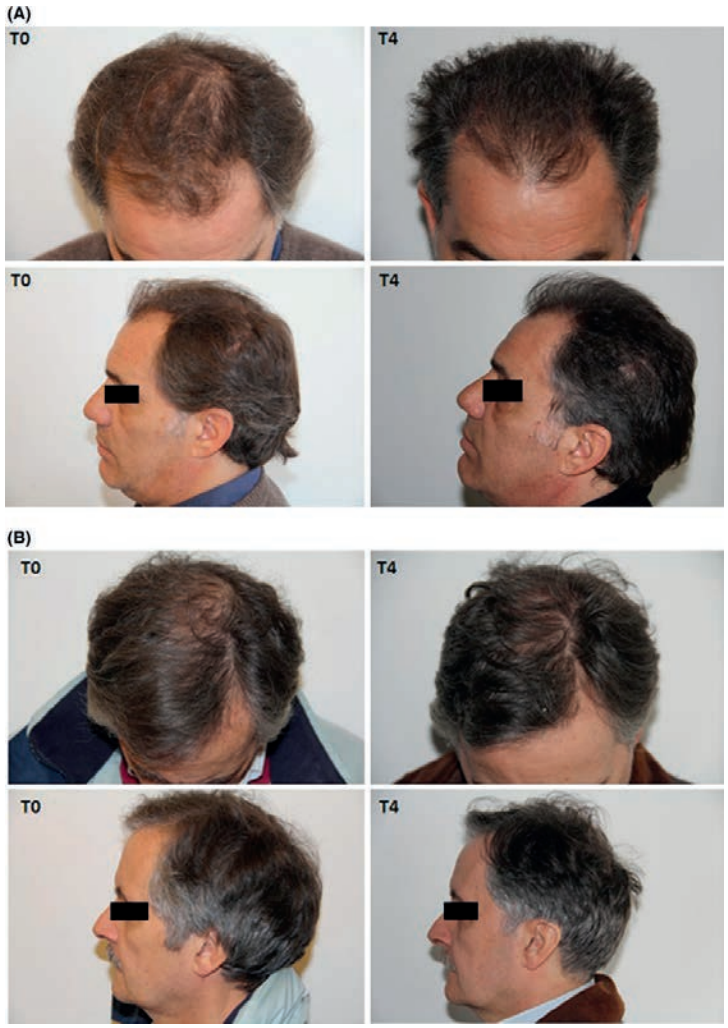

Fig. 5 Digital photography. *T0* baseline, *T4* 4 months (**a–c**)

Clinical Efficacy of a Cosmetic Treatment by Crescina® Human Follicle Stem Cell on Healthy Males with Androgenetic Alopecia

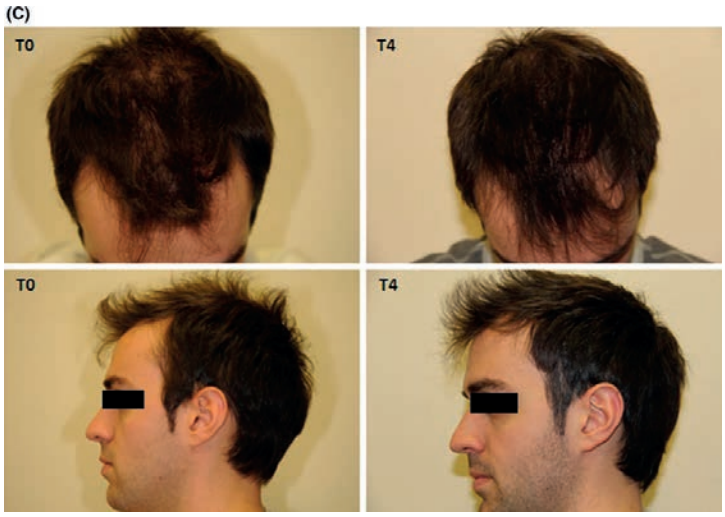

Fig. 5 continued

The present study aimed to assess the efficacy of the topical application of cysteine, lysine, a glycoprotein, hydrolyzed rice protein, and corosolic acid (the active ingredients that are contained in the formulation of Crescina® HFSC) in promoting hair growth and in decreasing hair loss [10]. It would be desirable to analyze a larger population sample; however, this would require longer-term studies (approximately 1 year), which are not always compatible with the needs of the economic commitment of research and the cosmetic market, which is rapidly and constantly developing. Moreover, the compliance of large groups of subjects who undergo the test decreases with time spent in the clinical trials. On this basis, as the present study has already shown efficacy in the short term (4 months), it was considered significant and important to highlight this positive result. The authors can further expand these data by considering a greater sample size and longer-term study.

In conclusion, the present investigation has demonstrated the effects of a mixture of ingredients that is able to promote hair growth and decrease hair loss. The results obtained showed that Crescina® HFSC applied for 4 months in subjects suffering from alopecia grade II to IV was effective in stimulating hair follicle activity as demonstrated by the time-dependent anagen rate increase. Correspondingly, the treatment decreased hair loss and hair resistance to traction, demonstrating its beneficial effect on hair loss.

ACKNOWLEDGMENTS

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Clinical Efficacy of a Cosmetic Treatment by Crescina® Human Follicle Stem Cell on Healthy Males with Androgenetic Alopecia

development. The performance of the study was sponsored by Labo Cosprophar AG, Basel, Switzerland. The sponsor had no influence in the performance, analysis, and interpretation of the study. Dr. Marzatico is the guarantor for this article, and takes responsibility for the integrity of the work as a whole.

Conflict of interest. Dr. Buonocore declares no conflict of interest. Dr. Nobile declares no conflict of interest. Dr. Michelotti declares no conflict of interest. Dr. Marzatico declares no conflict of interest.

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6. The Patents

Swiss and European Patents

- Swiss Patent CH 703 390
- Swiss Patent CH 711 466
- Swiss Patent CH 697 229
- Swiss Patent CH 693 815
- Swiss Patent CH 693 814
- Swiss Patent CH 693 816
- Swiss Patent CH 704 629
- EU Patent EP 2 561 858

SWISS
PATENT
CH 703 390

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Urkunde · Certificat · Certificato

über die Erteilung des Erfindungspatentes Nr.
de délivrance du brevet d'invention n°
di rilascio del brevetto d'invenzione no.

703 390

Nachdem die gesetzlichen Bedingungen erfüllt worden sind, ist für die in der beigefügten Patentschrift dargelegte Erfindung ein Patent mit der oben angegebenen Nummer erteilt worden.
Auf der ersten Seite der Patentschrift sind alle wesentlichen Angaben enthalten, die das vorliegende Erfindungspatent betreffen.
Erfindungspatente werden ohne Gewährleistung des Bundes erteilt. Massgeblich ist der Eintrag im Patentregister.

Bern, Datum der Patenterteilung

Les conditions requises par la loi étant remplies, un brevet portant le numéro susmentionné a été délivré pour l'invention décrite dans le fascicule ci-joint.
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Les brevets d'invention sont délivrés sans garantie de l'Etat. Seul l'enregistrement dans le registre des brevets fait foi.

Berne, date de la délivrance du brevet

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Berna, data del rilascio del brevetto

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Dr. Roland Grossenbacher

(19) SCHWEIZERISCHE EIDGENOSSENSCHAFT
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(11) CH 703 390 B1

(51) Int. Cl.: A61K 8/97 (2006.01)
A61Q 7/00 (2006.01)
A61P 17/14 (2006.01)
A61K 8/64 (2006.01)

Erfindungspatent für die Schweiz und Liechtenstein
Schweizerisch-liechtensteinischer Patentschutzvertrag vom 22. Dezember 1978

(12) PATENTSCHRIFT

(21) Anmeldenummer: 01304/11

(22) Anmeldedatum: 05.08.2011

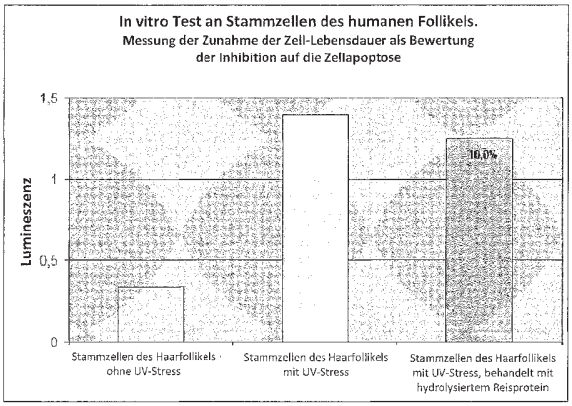
(24) Patent erteilt: 13.01.2012

(45) Patentschrift veröffentlicht: 13.01.2012

(54) Auf Haarfollikel-Stammzellen wirkende Zusammensetzung zur Stimulation des Haarwachstums.

(57) Eine auf Haarfollikelstammzellen wirkende Zusammensetzung zur Stimulation des Haarwachstums umfasst eine synergistische Kombination aus:
i) einer wirksamen Menge einer biologisch aktiven Komponente, welche die Expression von Proteinmarkern fördert, die mit dem Wachstum und der Proliferation von Follikelstammzellen assoziiert sind, und
ii) einer wirksamen Menge einer biologisch aktiven Komponente, welche die Proliferation von mesenchymalen Zellen der Hautpapille stimuliert, sowie einen kosmetisch annehmbaren Träger.

Dabei umfasst die biologisch aktive Komponente i) ein Peptid-Extrakt aus Reis, während die biologisch aktive Komponente ii) Corosolsäure umfasst.



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711 466

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Bern, Datum der Patenterteilung

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Berne, date de la délivrance du brevet

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Berna, data del rilascio del brevetto

Leiter Patente / chef des Brevets / capo dei Brevetti

Dr. Alban Fischer

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(19) SCHWEIZERISCHE EIDGENOSSENSCHAFT
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(11) **CH 711 466 B1**

(51) Int. Cl.: ***A61K 8/34*** *(2006.01)*

Erfindungspatent für die Schweiz und Liechtenstein
Schweizerisch-liechtensteinischer Patentschutzvertrag vom 22. Dezember 1978

(12) PATENTSCHRIFT

(21) Anmeldenummer: 01675/15

(22) Anmeldedatum: 17.11.2015

(24) Patent erteilt: 28.02.2017

(45) Patentschrift veröffentlicht: 28.02.2017

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(74) Vertreter:
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8038 Zürich (CH)

(54) Dermokosmetische Zusammensetzung zur topischen Anwendung mit penetrationsverstärkenden Eigenschaften und Verfahren zu deren Herstellung.

(57) Eine dermokosmetische Zusammensetzung zur topischen Anwendung und mit penetrationsverstärkenden Eigenschaften umfasst ein penetrationsverstärkendes System, welches Decylenglykol, Pentylenglykol und Caprylylglykol enthält, sowie eine oder mehrere dermokosmetisch aktive Substanzen und einen kosmetisch annehmbaren Träger. Eine Technologie bzw. ein transdermales Verfahren zur Penetration von dermokosmetischen Substanzen durch die Haut umfasst das Auswählen von kosmetisch aktiven Substanzen mit einem Molekulargewicht von ≤ 2000 Dalton; das Testen der kosmetisch aktiven Substanzen mit einem MG ≤ 2000 Dalton mittels einer Franz-Diffusionszelle und das Auswählen der kosmetisch aktiven Substanzen mit einem Absorptionsgradienten in die Dermis von weniger als 20% in 24 Stunden; das Zufügen eines vorzugsweise Decylenglykol, Pentylenglykol und Caprylylglykol umfassenden penetrationsverstärkenden Systems zu den ausgewählten kosmetisch aktiven Substanzen unter Bildung eines Gemisches; und das Zufügen eines kosmetisch annehmbaren Trägers zum besagten Gemisch.

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697 229

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Bern, Datum der Patenterteilung

Les conditions requises par la loi étant remplies, un brevet portant le numéro susmentionné a été délivré pour l'invention décrite dans le fascicule ci-joint.
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Berne, date de la délivrance du brevet

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Berna, data del rilascio del brevetto

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(19) SCHWEIZERISCHE EIDGENOSSENSCHAFT
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(11) **CH 697 229 B1**

(51) Int. Cl.: ***A61K 8/64*** *(2006.01)*
A61Q 7/00 *(2006.01)*

Erfindungspatent für die Schweiz und Liechtenstein
Patentschutzvertrag Schweiz-Liechtenstein vom 22. Dezember 1978

(12) PATENTSCHRIFT

(21) Anmeldenummer: 00072/08

(22) Anmeldedatum: 18.01.2008

(24) Erteilungsdatum: 31.07.2008

(45) Veröffentlichung der Anmeldung: 31.07.2008

(54) Haarlotion zur örtlichen Verwendung für den Haarneuwuchs.

(57) Potenzierte Haarlotion zur örtlichen Verwendung zur intensiven Reaktivierung des Haarwachstums bestehend aus einem Verband aus: Cystein, Lysin, Glycoprotein, Metaboli-sator, Zellproliferator.

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693 814

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Bern, Datum der Patenterteilung

Les conditions requises par la loi étant remplies, un brevet portant le numéro susmentionné a été délivré pour l'invention décrite dans le fascicule ci-joint.
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Berne, date de la délivrance du brevet

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Berna, data del rilascio del brevetto

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EIDGENÖSSISCHES INSTITUT FÜR GEISTIGES EIGENTUM

(11) **CH 693 814 A5**

(51) Int. Cl.[7]: **A 61 K 007/06**

Erfindungspatent für die Schweiz und Liechtenstein
Patentschutzvertrag Schweiz-Liechtenstein vom 22. Dezember 1978

(12) PATENTSCHRIFT A5

(21) Anmeldenummer: 01013/03

(22) Anmeldedatum: 10.06.2003

(24) Erteilungsdatum: 27.02.2004

(45) Veröffentlichung der Anmeldung: 27.02.2004

(54) Haarlotion zur örtlichen Verwendung für den Haarneuwuchs und die Verdickung des Haarschafts.

(57) Es wird eine Haarlotion zur örtlichen Anwendung zur Anregung des Haarneuwuchses beschrieben. Sie enthält einen Verband aus Zystein und/oder seinen Ne-benprodukten, Lysin und/oder seinen Nebenprodukten, einem Glycoprotein, dessen Zusammensetzung auch ein aus Serin und Threonin bestehendes Dipeptid vor-sieht.

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693 815

Nachdem die gesetzlichen Bedingungen erfüllt worden sind, ist für die in der beigefügten Patentschrift dargelegte Erfindung ein Patent mit der oben angegebenen Nummer erteilt worden.
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Erfindungspatente werden ohne Gewährleistung des Bundes erteilt. Massgeblich ist der Eintrag im Patentregister.

Bern, Datum der Patenterteilung

Les conditions requises par la loi étant remplies, un brevet portant le numéro susmentionné a été délivré pour l'invention décrite dans le fascicule ci-joint.
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Berne, date de la délivrance du brevet

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Berna, data del rilascio del brevetto

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Dr. Roland Grossenbacher

(19) SCHWEIZERISCHE EIDGENOSSENSCHAFT
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(11) **CH 693 815 A5**

(51) Int. Cl.[7]: **A 61 K 007/06**

Erfindungspatent für die Schweiz und Liechtenstein
Patentschutzvertrag Schweiz-Liechtenstein vom 22. Dezember 1978

(12) PATENTSCHRIFT A5

(21) Anmeldenummer: 01014/03

(22) Anmeldedatum: 10.06.2003

(24) Erteilungsdatum: 27.02.2004

(45) Veröffentlichung der Anmeldung: 27.02.2004

(54) Haarlotion zur örtlichen Verwendung für den Haarneuwuchs mit Langzeitwirkung.

(57) Es wird eine Haarlotion zur örtlichen Anwendung zur Anregung des Haarneuwuchses beschrieben. Sie enthält einen Verband aus Zystein und/oder seinen Ne-benprodukten, Lysin und/oder seinen Nebenprodukten und einem Glycoprotein, dessen Zusammensetzung auch Zyclodextrine vorsieht.

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693 816

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Berna, data del rilascio del brevetto

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(19) SCHWEIZERISCHE EIDGENOSSENSCHAFT
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(11) **CH 693 816 A5**

(51) Int. Cl.[7]: **A 61 K 007/06**

Erfindungspatent für die Schweiz und Liechtenstein
Patentschutzvertrag Schweiz-Liechtenstein vom 22. Dezember 1978

(12) PATENTSCHRIFT A5

(21) Anmeldenummer: 01015/03

(22) Anmeldedatum: 10.06.2003

(24) Erteilungsdatum: 27.02.2004

(45) Veröffentlichung der Anmeldung: 27.02.2004

(54) Haarlotion für den Haarneuwuchs und zur Behandlung der Follikeleinheiten.

(57) Es wird eine Haarlotion zur örtlichen Anwendung zur Anregung des Haarneuwuchses beschrieben. Sie enthält einen Verband aus Zystein und/oder seinen Ne-benprodukten, Lysin und/oder seinen Nebenprodukten, einem Glycoprotein, einem aus Serin und Threonin be-stehendem Dipeptid und einem Vasodilatator, in dem der vasodilatatorische Wirkstoff je nach Gewicht des zuvor genannten Verbands zwischen 45 % und 85 % anwesend ist und die Zusammensetzung der Lotion auch ein weiteres Glycoprotein, das so genannte Pro-tobulbina enthält, das durch die aerobe Fermentation von Hefe der Art Saccharomices cerevisiae produziert.

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704 629

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Bern, Datum der Patenterteilung

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Berna, data del rilascio del brevetto

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(11) **CH 704 629 B1**

(51) Int. Cl.: ***A61K 8/64*** *(2006.01)*
A61K 8/96 *(2006.01)*

Erfindungspatent für die Schweiz und Liechtenstein
Schweizerisch-liechtensteinischer Patentschutzvertrag vom 22. Dezember 1978

(12) PATENTSCHRIFT

(21) Anmeldenummer: 00077/12

(22) Anmeldedatum: 17.01.2012

(24) Patent erteilt: 28.09.2012

(45) Patentschrift veröffentlicht: 28.09.2012

(54) Auf Stammzellen der Epidermis und Dermis und auf deren Mikro-Umgebung wirkende kosmetische Zusammensetzung.

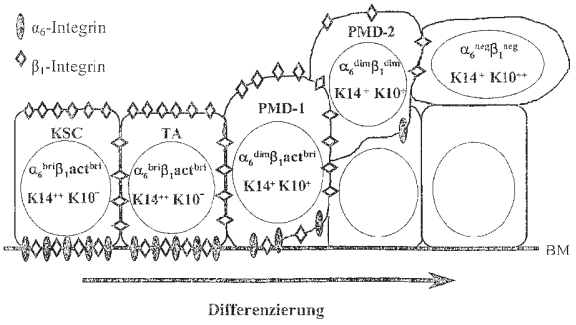
(57) Eine auf Stammzellen der Epidermis und/oder der Dermis und/oder auf deren Mikro-Umgebung, der Gesichts-/Körperhaut und/oder der Kopfhaut wirkende kosmetische Zusammensetzung umfasst:

a) ein auf die Stammzellen der Epidermis (EpiSC) biologisch wirkendes Pentapeptid,

b) eine auf EpiSC biologisch wirkende Peptid-Fraktion aus Erbsen (Pisum sativum L.) mit einem Molekulargewicht von 2000 bis 5000 Dalton,

c) ein auf EpiSC biologisch wirkendes Extrakt aus der Alge Laminaria digitata, sowie einen kosmetisch annehmbaren Träger.

Die kosmetische Zusammensetzung ist zur Behandlung oder Prävention von Anzeichen der Hautalterung und/oder zur Unterstützung des physiologischen Haarwachstums geeignet.



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Es wird hiermit bescheinigt, dass für die in der Patentschrift beschriebene Erfindung ein europäisches Patent für die in der Patentschrift bezeichneten Vertragsstaaten erteilt worden ist.

CERTIFICATE

It is hereby certified that a European patent has been granted in respect of the invention described in the patent specification for the Contracting States designated in the specification.

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Europäisches Patent Nr. / European patent No. / Brevet européen nº

2561858

Patentinhaber / Proprietor of the patent / Titulaire du brevet

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München, den / Munich, / Fait à Munich, le 06.04.16

Benoît Battistelli
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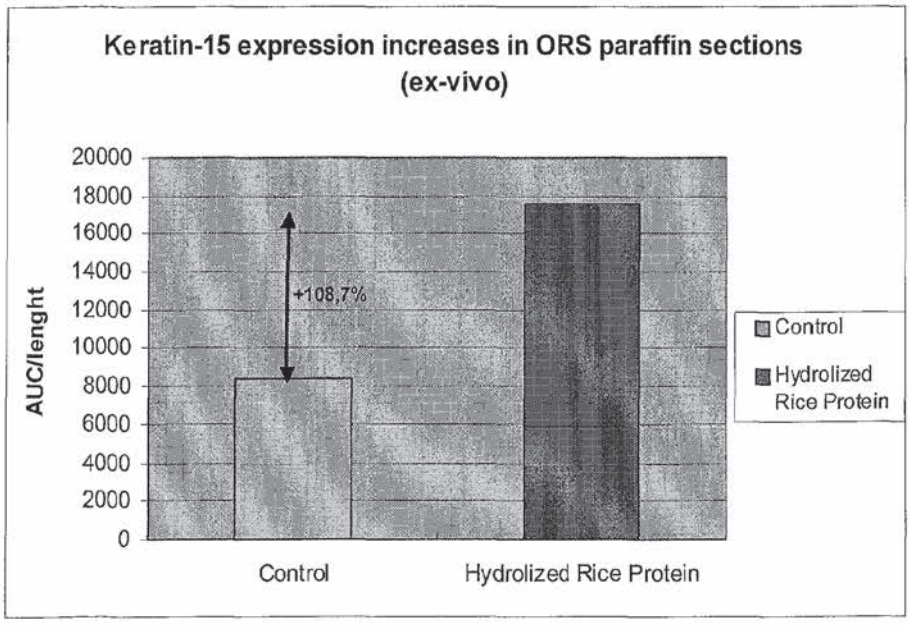
(71) Applicant: **LABO Cosprophar AG**
4052 Basel (CH)

(54) A composition for activating hair follicle stem cells to stimulate hair growth

(57) The present invention concerns a cosmetic composition for activating hair follicle stem cells to stimulate hair growth comprising the synergistic association of a biologically active component that promotes the expression of marker proteins associated with the growth and proliferation of follicle stem cells and a biologically active component that stimulates the proliferation of the mesenchymal cells of the dermal papilla and a cosmetically acceptable carrier.

FIG. 1



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7. Points of Sale

Crescina Display at the Pharmacy

LABO
LABO COSPROPHAR

SWISS PATENT CH 703 390

Points of Sale

LCX, Hong Kong

Lord & Taylor, New York

Counter at Pondok Indah Mall, Jakarta

Beautiqa Store, Manila

Ave Pharmacy, Moscow

Points of Sale

Ave Pharmacy, Moscow

Sensiblu Pharmacy, Bucharest

BinSina Pharmacy, Dubai

Ave Pharmacy, Moscow

Kanaki Fotini Pharmacy, Athens

Zaytouna Pharmacy, Beirut

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SWISS
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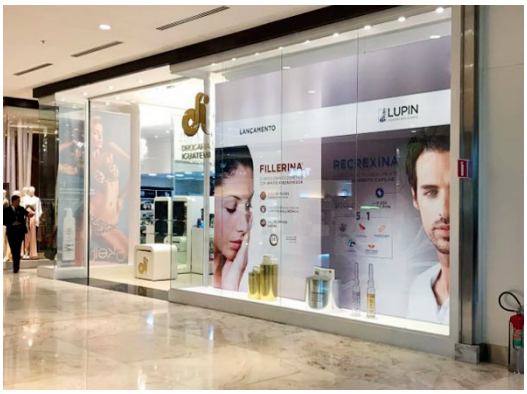
CH 703 390

Points of Sale

John Bell & Croyden, London

Apotheek Libra, Houthalen

Kanaki Fotini Pharmacy, Athens



Drogaria Iguatemi, São Paulo

The SM Store at Aura Premier, Manila

Kohl's, New York

8. P.O.S. Materials

P.O.S. Materials
Thinometer

P.O.S. Materials

Window Card

P.O.S. Materials

Flyer Thinometer

SWISS PATENT CH 703 390

LABO COSPROPHAR

P.O.S. Materials

Free Samples (Man / Woman)

Consumer Leaflet

CRESCINA®

RE-GROWTH

HFSC

TRANSDERMIC TECHNOLOGY

SWISS AND EUROPEAN PATENTS

SWISS PATENT CH 703 390

SWISS PATENT CH 711 466

SWISS PATENT CH 697 229

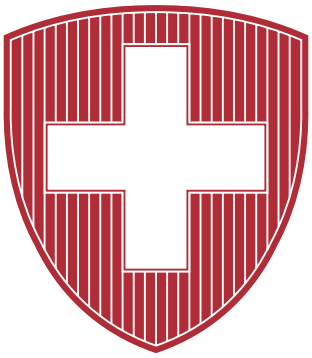
SWISS PATENT CH 693 815

SWISS PATENT CH 693 814

SWISS PATENT CH 693 816

SWISS PATENT CH 704 629

EU PATENT EP 2 561 858



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