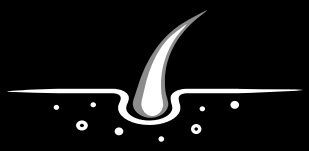
Morgan's
Since 1873

Hair Growth Product Range



Cosmetic Ingredient Dossier:

- 3-5% Redensyl
- 4% Anagain
- 2-3% ACB Pea Peptide
- Caffeine Extract
- Rosemary Extract
- Nettle Extract
- Horsetail Extract

Hair Growth Range Ingredient Highlights

Hair loss affects both women and men. It is mainly caused by an imbalance of the hair growth cycle leading to a reduced number of growing ('anagen') hair combined with an increased number of degenerating ('telogen') ones. Morgan's has developed a new range of products using a selection of only the best ingredients shown to combat hair loss.

Main Active Ingredients:

3-5% REDENSYL ™ Shown to dramatically reactivates hair growth and decreases hair loss with clinically visible results in 3 months by: 1) Re-launching stem cells activity and proliferation. When the outer root sheath stem cells (ORSc) are vitalized they trigger a new hair cycle; 2) Increasing the dermal papilla's fibroblasts metabolism. When hair follicles are nourished it results in the stem cells switching on the anagen phase faster. The efficiency of Redensyl™ at 3% was evaluated in double-blind tests vs a placebo. The results showed after 3 months increased length of anagen phase by 9% and decrease of telogen phase by 17%. Overall 85% of volunteers showed clinical improvements: More anagen hair, a higher density, more visible hair.

4% ANAGAIN ™ - An Organic Pea Sprout Extract to Rebalance the Hair Life Cycle. Based on sprouts of organic pea, AnaGain™ reduces hair loss by inducing dermal papilla cells to reactivate hair growth. Studies shows that when used in the recommended range (2 - 4%) Anagain can: 1) Stimulate hair growth at the root; 2) Prolong the life cycle of hair; 3) Fully restore the vitality of the hair; 4) Achieve denser hair in just 3 months.

2-3% ACB Pea Peptides - ACB Pisum Sativum Peptide provides volume and antioxidant protection by offsetting the symptoms of hair aging. It reduces the damage caused by free radicals to promote scalp and follicle health essential producing youthful, voluminous looking hair. Test results indicate that 2.0% ACB Pisum Sativum Peptide provides visible thickening benefits to the hair.

Caffeine Extract - In recent years, caffeine has demonstrated potential as a treatment for AGA [Androgenic Alopecia]. Due to being a phosphodiesterase inhibitor, caffeine increases cyclic adenosine monophosphate levels in cells and consequently promotes cell proliferation through stimulating cell metabolism - a mechanism that may counteract testosterone/dihydrotestosterone-induced miniaturization of the hair follicle. Caffeine also resulted in increased expression of insulin-like growth factor-1, a promoter of hair growth, in both male and female hair follicles.

Horsetail Extract - Derived from the Equisetum Arvense plant, commonly known as horsetail. Rich in beneficial compounds such as silica, selenium and antioxidants. Strengthens and improves the elasticity of the hair fiber, helps regulate the hair growth cycle, and reduces inflammation and improves cell turnover to create an optimal environment on the scalp for healthy hair growth.

Rosemary Extract - Rosmarinus officinalis is a medicinal plant with diverse activities including enhancement microcapillary perfusion. Studies aimed at investigating the clinical efficacy of rosemary oil in the treatment of androgenetic alopecia (AGA) and compare its effects with minoxidil 2%. Both groups experienced a significant increase in hair count at the 6-month endpoint compared with the baseline and 3-month endpoint The findings provided positive evidence with respect to the efficacy of rosemary oil in the treatment of AGA.

Nettle Extract – Scientific study in this area is still limited but Nettle root (Urtica dioica) is thought to increase hair growth through numerous processes: DHT suppression, anti-inflammatory effects, better blood circulation, vitamin content and sebum reduction. Nettle root contains anti-inflammatory chemicals that reduce scalp irritation that can disrupt the hair growth cycle and contribute to hair loss. It also has antimicrobial properties and capacity to inhibit the enzyme 5-alpha-reductase is (one of the key reasons postulated for its advantage for hair growth). Nettle root contains vitamins (such as A and C), minerals (such as iron and magnesium), and other bioactive substances that are beneficial to general hair health.

Morgan's Hair Growth Range: Benefits, Uses, How to Use and FAQs

Are you stressed with hair fall? Is it taking a toll on your confidence? Don't want to spend money on a hair transplant? An excellent alternative to hair transplant is the new '**Morgan**'s **Hair Growth**' range of products. Combining popular and clinically proven ingredients to tackle hair loss effectively. It is made of a newly discovered plant-based compounds, including Redensyl (based around the molecule 'Dihydro Quercetin-Glucoside or DHQG'), which aids in hair regrowth, also Anagain, Pea Peptides and a selection of natural extracts and vitamins.

Morgan's Hair Growth range uses the top hair growth-promoting compounds that works on two key aspects: reducing hair loss and accelerating new hair growth. It accomplishes this by explicitly targeting the stem cells found within hair follicles and stimulating their growth cycle.

How Does it Work?

Our hair growth cycle consists of 3 stages, they are:

- **Anagen Phase** - The phase of hair growth.
- **Catagen Phase** - The phase of hair transition.
- **Telogen Phase** - The phase of hair loss.

4-Step Plan

1. Ensures Faster Hair Growth: stimulates the first phase of hair growth to reactivate hair cell division, resulting in hair growth.

2. Prevents Hair Loss: According to a study, after just three months of use, hair fall is substantially reduced by 17%. Additionally, it lessens the telogen phase's negative impacts by more than 16%. Your hair doesn't break as easily now that redensyl provides thicker hair development and improved scalp nourishment.

3. Increasing Hair Thickness and Strength: It nourishes the hair follicles with nutrients and improves blood circulation in the scalp.

4. It Boosts Hair Density: Redensyl and Anagain have been known for reducing hair thinning by boosting hair density. During the anagen phase, hair growth has increased.

Benefits of 'Morgan's Hair Growth Range' for Hair

1. Promotes Hair Growth: We use ingredients known for extending the anagen phase of the hair growth cycle, which is the active phase where hair grows. By promoting hair follicle activity and reducing hair loss during the telogen phase, our products can accelerate hair growth, resulting in thicker and fuller hair.

2. Strengthen and Thicken Hair Strands: Regular use can improve the structural integrity of hair strands. It helps strengthen the hair shafts, making them more resistant to breakage and damage. This leads to thicker and healthier-looking hair.

3. Improve Blood Circulation to the Scalp: Increases blood circulation to the scalp, ensuring that hair follicles receive an adequate supply of nutrients and oxygen. Improved blood flow nourishes the follicles and produces an environment suitable for hair development.

4. Nourish Hair Follicles: Provides vital nutrients to hair follicles, supporting their health and vitality. By nourishing the follicles, Morgan's Hair Growth Range helps maintain their functionality and promotes optimal hair growth.

5. Anti-Inflammatory Properties: Ingredients that possess anti-inflammatory properties, which can help soothe the scalp and reduce potential inflammation. This is particularly beneficial for individuals with scalp conditions or sensitivities.

6. Improves Hair Gloss and Appearance: Regular use can enhance the overall appearance of the hair. It can contribute to improved hair texture, shine, and vibrancy, making the hair look healthier and more attractive.

7. Hair Fall Reduced: Redensyl targets the hair follicles' stem cells, promoting their division and activation. Combined with Anagain this action helps reduce hair loss by prolonging the anagen phase and minimizing the duration of the telogen phase when hair shedding occurs.

8. Suitable for All Hair Types: Morgan's Hair Growth Range is compatible with different hair types, including straight, curly, wavy, and textured hair. It can benefit both men and women experiencing hair loss or thinning.

9. Natural and Non-hormonal Therapy: Morgan's Hair Growth Range is a better option for people who prefer natural options because it is a non-hormonal therapy option for hair loss. It utilizes the ability of substances produced by plants to promote hair growth without disrupting hormonal balance.

10. Convenience and Versatility: Morgan's Hair Growth Range's water-soluble nature allows for easy application, providing users with convenient options to integrate it into their normal hair care routine. Available in serum, mousse and spray for ultimate convenience.

Side Effects: Clinical research of the ingredients and product safety report doesn't indicate any negative side effects. It promotes hair growth, delivers outstanding results without having any negative effects.

FAQs

Q) Is it safe?

A) Yes, it is risk-free alternative for hair transplants. It contains plant components that promote hair development. Furthermore, research reveals minimal negative effects and shows visible results.

Q) What is it made from?

A) The products is a combination Redensyl, Anagain, Pea Peptides and natural extracts. Redensyl is composed of pure plant extracts such as DHQG, EGCG 2, Glycine, Zinc Chloride, and Meta-bisulfit. Anagain is composed of Pisum Sativum (Pea) Sprout Extract

Q) How long should I use Redensyl for visible results?

A) You should consistently use redensyl for 5-6 months for visible results.

Q) Has anyone used Morgan's Hair Growth Range for hair loss?

A) Yes, some people have used our products for Hair Loss and reported positive results after only 4-6 months of consistent use.

REDENSYL™

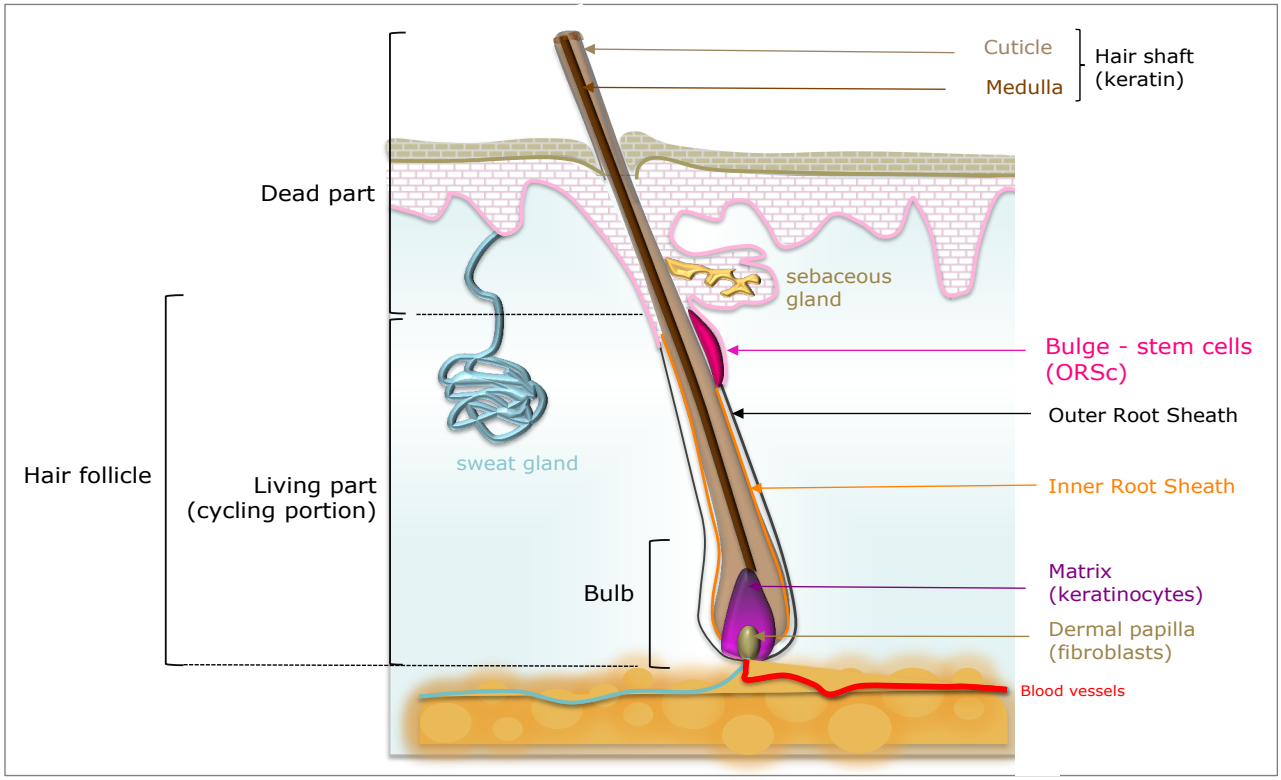
Morgan's Since 1873

Hair: continuously self-regenerating

- The full head of hair consists of 110,000 - 150,000 hairs
- The average of scalp surface is 600 cm^2 [1,2]
- Each hair is produced by a single hair follicle
- Each hair follicle produces an average of 30 hairs during our life
- Hair grows at 1 cm per month which corresponds to:
  - 0.3 to 0.5 mm per day
  - about 10 cm per year
- We lose naturally from 50 to 100 hair each day.

The hair structure is divided in 2 sections: the hair follicle and the hair shaft

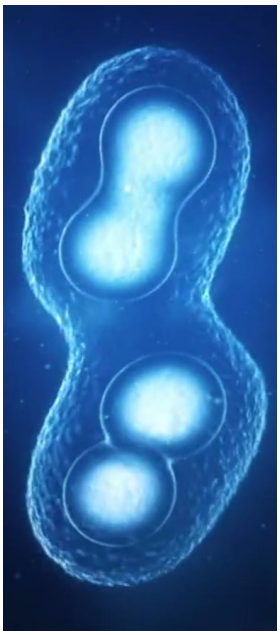
Zoom on the hair structure



REDENSYL™

Morgan's Since 1873

What are Stem Cells



Stem cells are non differentiated cells

They have two key features:

- Self renewal: they can give birth to other stem cells
- Potency: they can give birth to specialized cell types

Stem cells are divided in two broad categories:

- Embryonic stem cells, which are totipotent: they can create a complete human being
- Adult stem cells, which are multipotent: they can generate an organ

Stem cells are at the origin of our body self regeneration faculties.

Stem cells in regenerative medicine

Stem cells therapy has been a key fundamental research area for more than 30 years.

Concept: introduce new adult stem cells into damaged tissues and organs to regenerate them

Targeted diseases:

- Leukemia (bone marrow)
- Parkinson's and Alzheimer's diseases (neurons)
- Type I diabetes (pancreas)
- Cancers (brain)
- Heart failure (heart)
- Muscles atrophy (muscles)
- Wound healing (skin)
- Baldness (hair) [1]

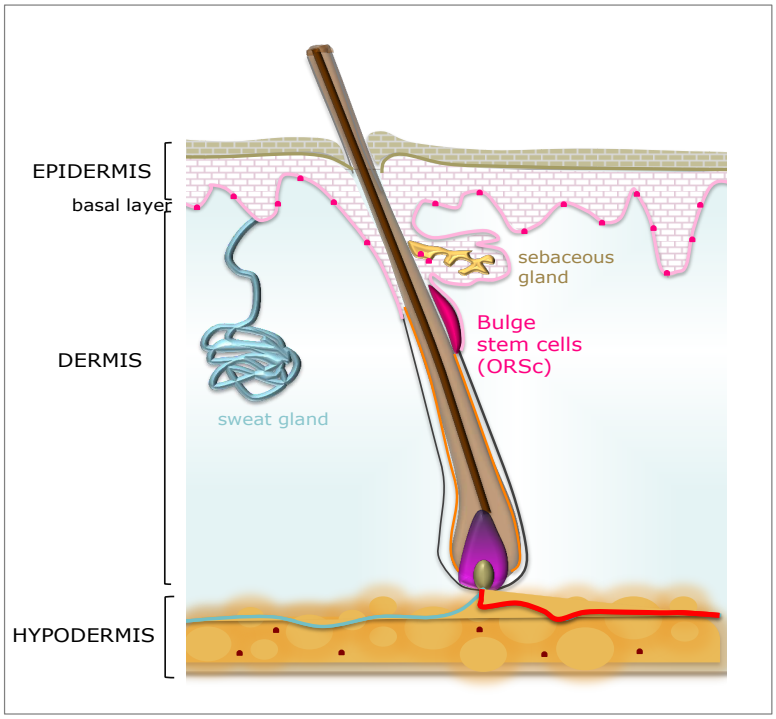
In 2013, 500 clinical trials based on stem cells therapy have been initiated [2]

[1] Yang et al. Nature Communications, 2014
[2] www.clinicaltrials.gov

Stem cells in skin

Stem cells are mainly found in

- The hypodermis
- The basal layer
- The sebaceous gland
- The bulge (ORSc stem cells)

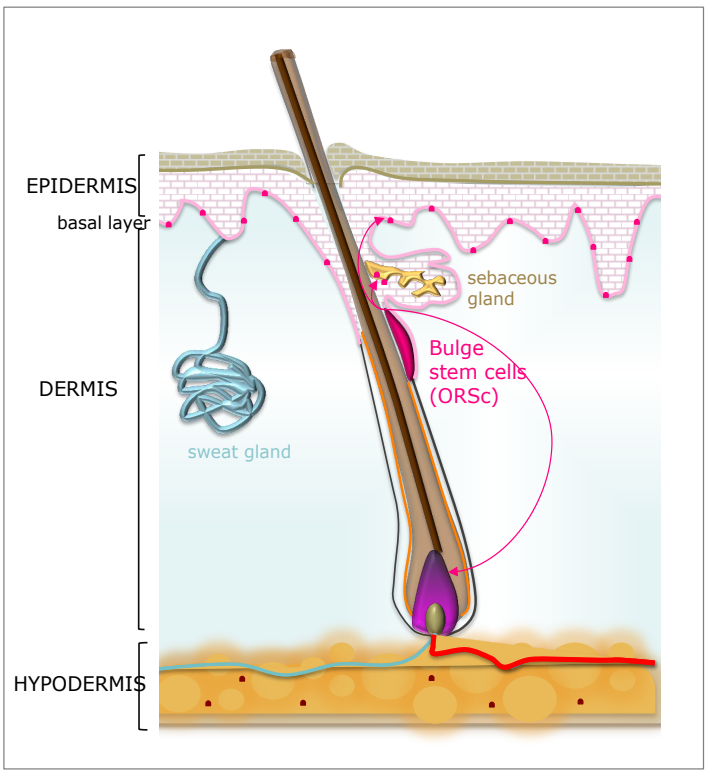


Diaz-Flores, 2006, Histol Histopathol.

Bulge stem cells (ORSc)

Bulge stem cells are mother cells, generating:

- the epidermis cells,
- the hair follicle matrix,
- the sebaceous gland stem cells.



Diaz-Flores, 2006, Histol Histopathol.

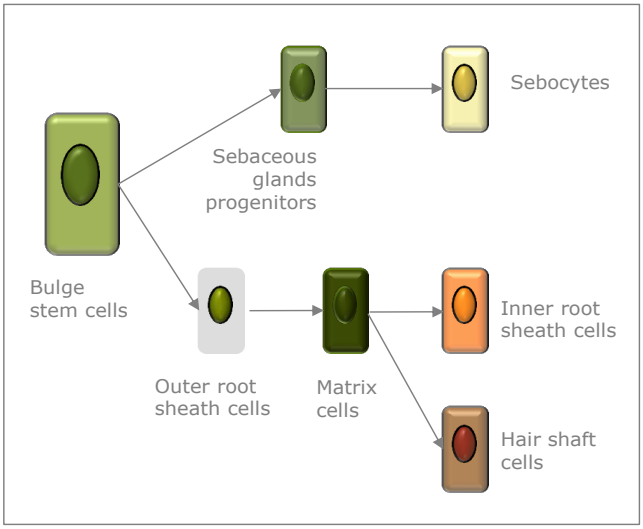
REDENSYL™

Bulge stem cells (ORSc)

Bulge stem cells are expressing the keratin 15 marker.

They have a key role in the regeneration of the hair follicle.

Bulge stem cells are initiating the hair cycle.



THE HAIR CYCLE IS DIVIDED IN 3 STEPS

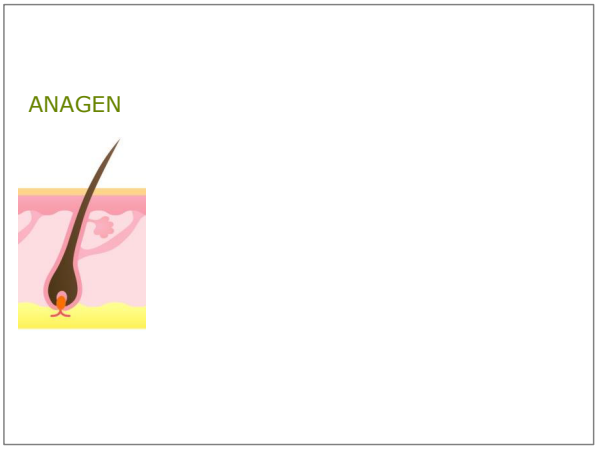
Step 1: ANAGEN - Growing phase

Anagen phase is the active phase of the hair (80% to 90% of all hair).

Keratinocytes in the matrix at the root of the hair are dividing rapidly.

During this phase the hair grow about 1 cm every month.

Scalp hair stays in this active phase of growth for 2-6 years.



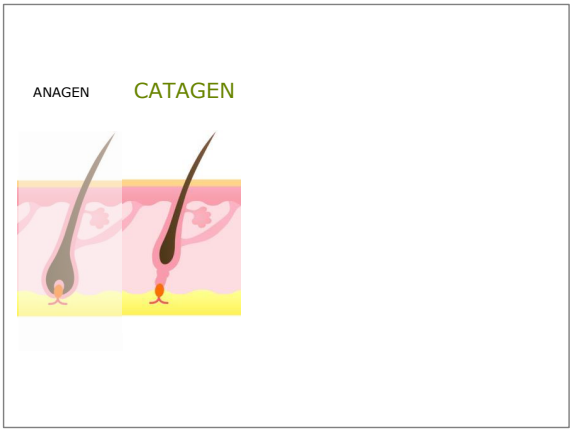
Randall 2009. The biology of hair growth, Gurpreet S. Ahluwalia (ed.), Cosmetic Applications of Laser and Light-Based Systems, 3-35, William Andrew Inc.

Step 2: CATAGEN - Transition phase

Catagen phase is a transitional stage and 2% of all hairs are in this phase.

This phase lasts for about 2-3 weeks.

During this phase, hair growth stops.



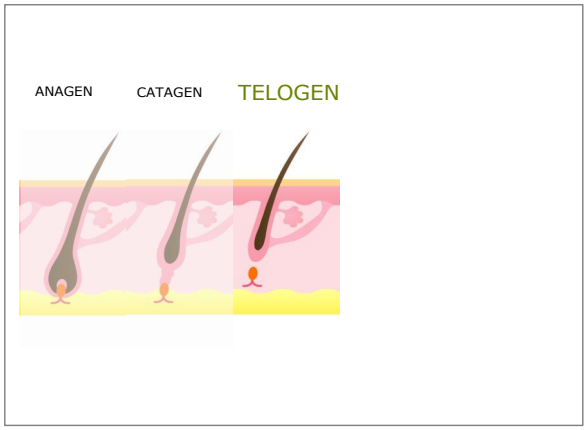
Step 3: TELOGEN - Falling phase

Telogen phase is the resting phase and accounts for 10-15% of all hairs.

This phase lasts for about 3 months.

During this phase the hair follicle is at rest and the club hair is completely formed.

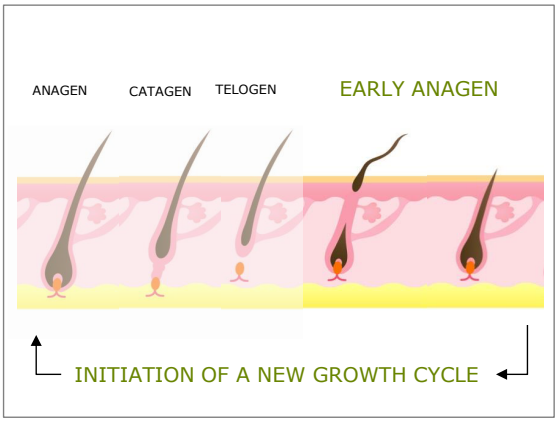
During a period of intensive hair loss, up to 30% of the hairs can be in the telogen phase.



Transition to a new cycle

Early Anagen phase is the activation of a new hair cycle growth.

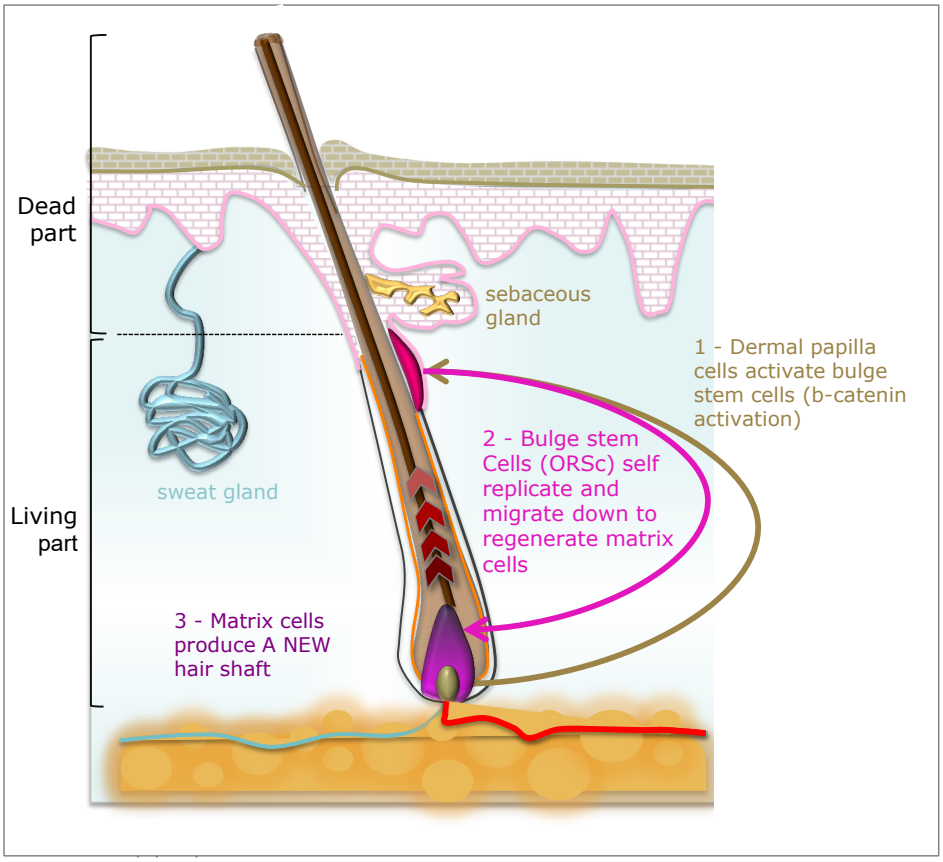
A new hair is formed and pushes the club hair up the follicle and eventually out.



Early anagen: chronology of the communication

Cells from the dermal papilla activate bulge stem cells (transient activation of the ß-catenin pathway initiates the anagen phase to induce new hair follicle [1,2]).

Bulge stem cells self replicate and migrate into the matrix to create new active keratinocytes.



[1] Lo Celso et al, 2004
[2] Shimizu and Morgan, 2004

What happens during hair loss?

Hair loss is a biological problem.

It happens when the number of hairs in anagen phase is lower than those in the telogen phase.

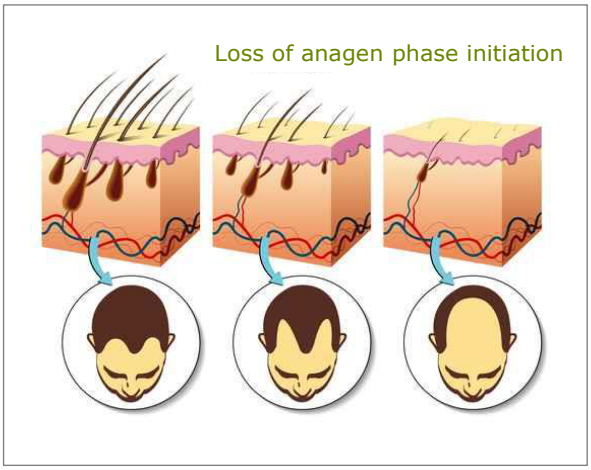
40% of men will have noticeable hair loss (alopecia) by age 35. It reaches 65% by 60 years of age.

50 to 75% of women suffer noticeable hair loss by age 65.

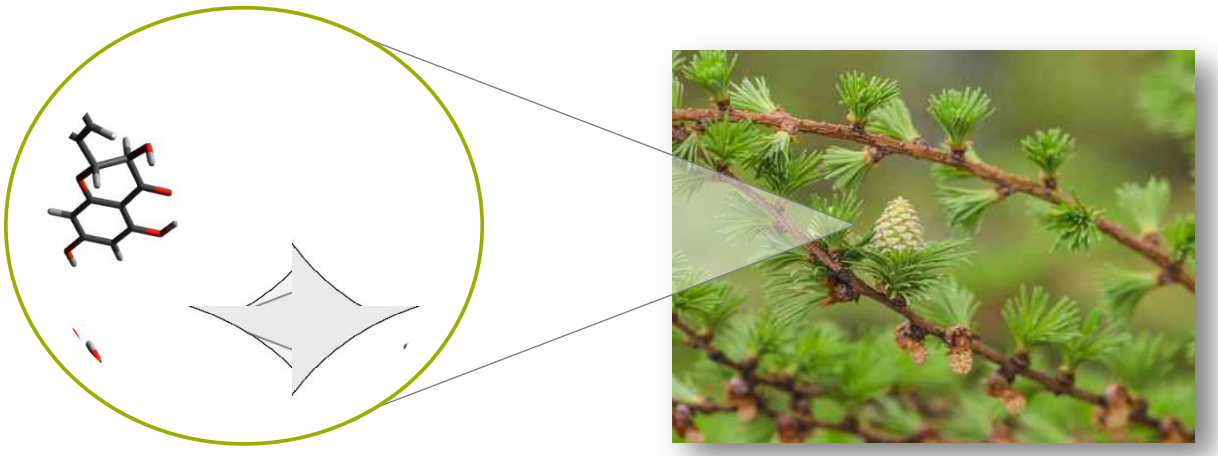
Hair loss has several origins[1]:

- Hormones (androgenic alopecia)
- Stress
- Aging
- Infections

No matter the causes, hair loss happens when the initiation of the new anagen phase (activation of ORS stem cells) is not activated.



DHQG: Dihydroquercetin-glucoside



Origin: Larch tree

MW: 466 g/mol

Biotechnology optimisation (glycosylation)

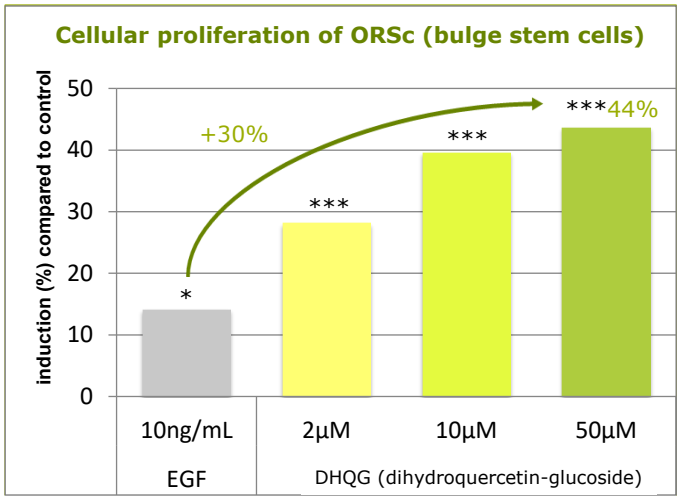
REDENSYL™

Morgan's Since 1873

DHQG: activation of bulge stem cells (*in vitro*)

PROTOCOL:

Incubation of human ORS stem cells (hair follicle bulge stem cells) with increasing concentrations of dihydroquercetin-glucoside (DHQG).



*p<0.01, ***p<0.001 compared to control, Student's t Test

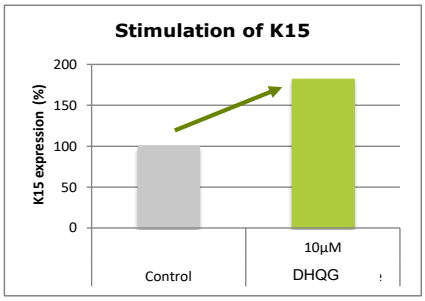
- DHQG enhances the division of the hair follicle ORS stem cells

(Nota: 50µM DHQG = 1/3 of the amount tested in the clinical assessment)

DHQG: effects on hair follicle stem cells genes (*in vitro*)

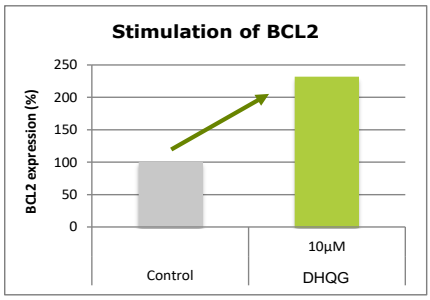
PROTOCOL:

Incubation of human ORS stem cells (hair follicle bulge stem cells) with different concentrations of dihydroquercetin-glucoside (DHQG). Measure of mRNA expression using qRT-PCR of markers of stem cells' phenotype (K15), anti-apoptosis (BCL2) and differentiation (β-catenin).



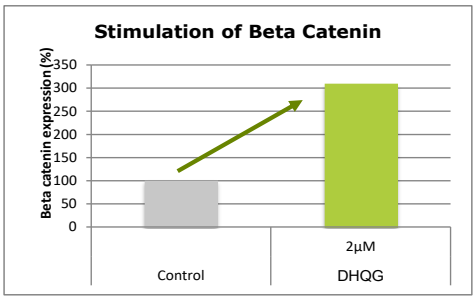
Stimulation of the expression of cytokeratin 15

- DHQG maintains the hair follicle stem cells' phenotype



Stimulation of the expression of BCL2 marker

- DHQG protects the hair follicle stem cells from apoptosis



Stimulation of the expression of the beta-catenin marker

- DHQG stimulates the hair follicle stem cells to initiate the anagen phase

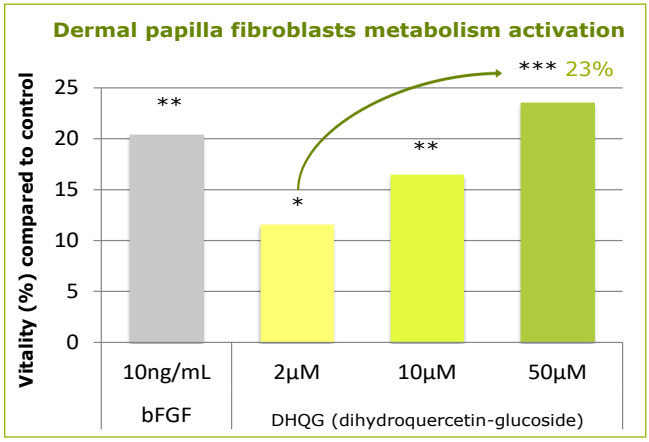
DHQG: stimulation of dermal papilla cells metabolism (*in vitro*)

PROTOCOL:

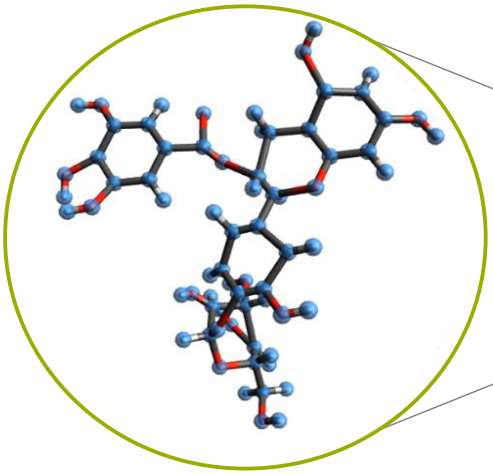
Incubation of human fibroblasts dermal papilla cells (HFDPc) with increasing concentrations of dihydroquercetin-glucoside (DHQG).

- DHQG activates the metabolic activity of HFDPc, for a better nourishment of the hair follicle

(Nota: 50µM DHQG = 1/3 of the amount tested in the clinical assessment)



EGCG2: Epigallocatechin-gallate-glucoside



Origin: Green tea leaves

MW: 604 g/mol

Biotechnology optimisation (glycosylation)

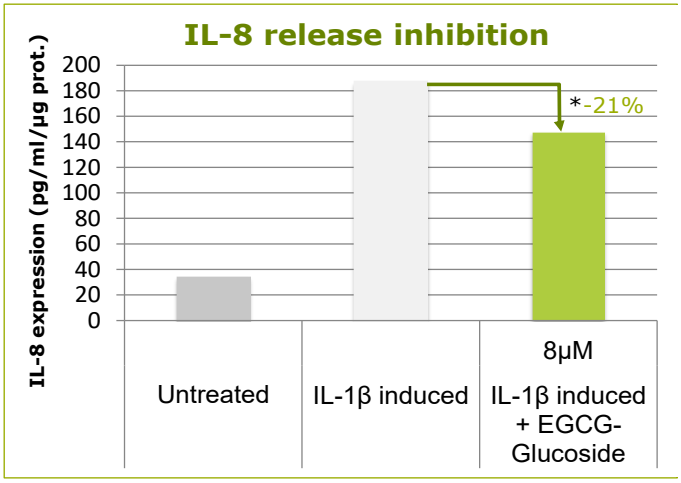
EGCG2: inhibition of interleukin 8 release (*in vitro*)

PROTOCOL:

Incubation of human normal keratinocytes with epigallocatechin gallate-glucoside (EGCG2). Measure of interleukin 8 release after induction by IL-1b.

- EGCG2 inhibits the release of interleukin 8, a cytokine involved in hair loss (Kuwano 2007. Br J Dermatol)

(Nota: 8µM EGCG2 = 1/2 of the amount tested in the clinical assessment)



*p<0.05 compared to control, Student's t Test

Creation of Redensyl™

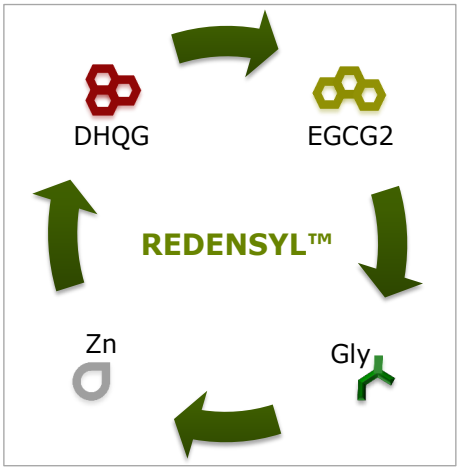
Based on these research results we combined:

DHQG
- Activator of stem cell division
- Maintenance of their stem cell properties
- Protection against apoptosis
- Stimulation of dermal fibroblasts metabolism

EGCG2
- Highly potent antioxidant
- Inhibitor of interleukin 8 release

Zinc, because
- Zn increases incorporation of cystine in hair proteins[1]
- Deficiency in zinc is associated with hair loss

Glycine, one of the top 10 amino acid in hair
- The main structural proteins in the hair fiber are the hair keratins and the hair keratin-associated proteins, KAPs
- The KAPs possess either high cysteine or high glycine-tyrosine content [2]

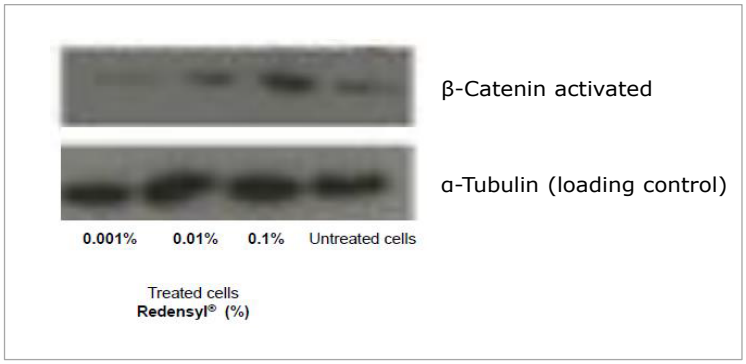


[1] Hsu et al., 1971, J. Nutr. 101.
[2] Rogers et al., 2002, JBC Papers in Press.

Redensyl™: Activation of β-Catenin (*in vitro*)

PROTOCOL:

Western blot analysis run on human androgenic alopecic ORSc (3 donors) treated with Redensyl™. Measurement of β-Catenin activation.



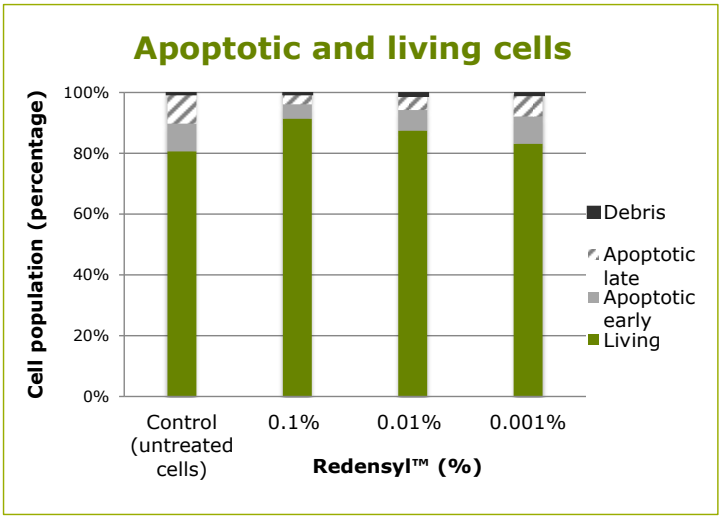
• Redensyl™ activates β-Catenin in androgenic alopecia ORSc which confirms the very good results observed during the q-RT PCR with DHQG.

EGCG2: inhibition of interleukin 8 release (*in vitro*)

PROTOCOL:

Apoptosis Annexin V assay run on human androgenic alopecic ORSc (3 donors) treated with Redensyl™. Measurement of living cells situation proportions.

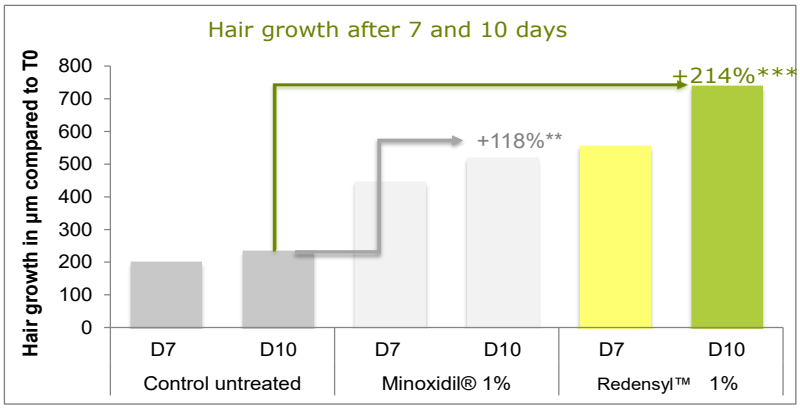
• Redensyl™ protects androgenic alopecia ORSc from apoptosis which confirms the very good results observed during the q-RT PCR with DHQG.

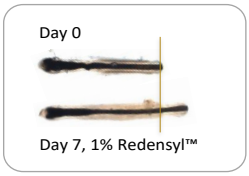


Hair follicle growth test (Philpott test)

PROTOCOL:

24 hair follicles from men suffering from alopecia were maintained alive with either 1% of Minoxidil or 1% of Redensyl™ during 10 days. Hair growth was measured at D7 and D10.





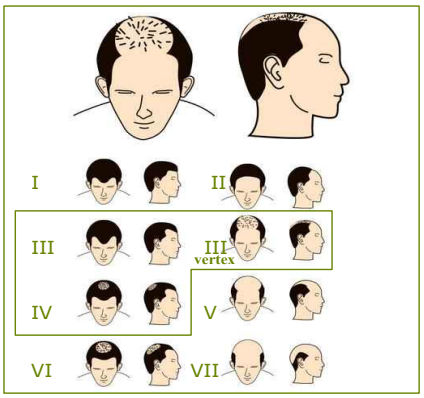
**p<0.1, ***p<0.001 compared to untreated, Student's t Test

- Redensyl™ increases hair growth by +214% compared to untreated
- Redensyl™ acts almost 2x more than Minoxidil, the benchmark reference.

Protocol of clinical trial

VOLUNTEERS

- 26 men aged 18 to 70 years old
- Brown to dark hair
- Qualified for a grade 3 to 4 alopecia (Norwood scale)
- With minimum 150 hair/cm2 and 40 telogen hairs/cm2

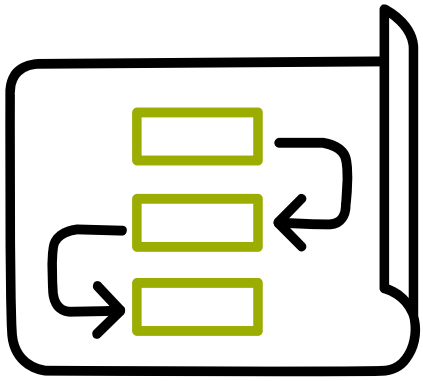


PROTOCOL

- Double blind clinical trial versus a placebo
- Applying the formula once a day
- 50% of volunteers received the placebo
- 50% received the formula with 3% Redensyl™
- Clinical study was performed under the control of a dermatologist.
- Period of the test: autumn

Clinical formula: AQUA, ALCOHOL DENAT., BUTYLENE GLYCOL, GLYCERIN, XANTHAN GUM, DISODIUM EDTA, CITRIC ACID, (+/-) REDENSYL™ 3%

Evaluated parameters



Clinical measures at D0, D30 and D84

- Macro pictures on scalp
- Density of hair in anagen phase
- Density of hair in telogen phase
- Ratio anagen/telogen
- Pictures of the head
- Self assessment questionnaire at D84

Nota:

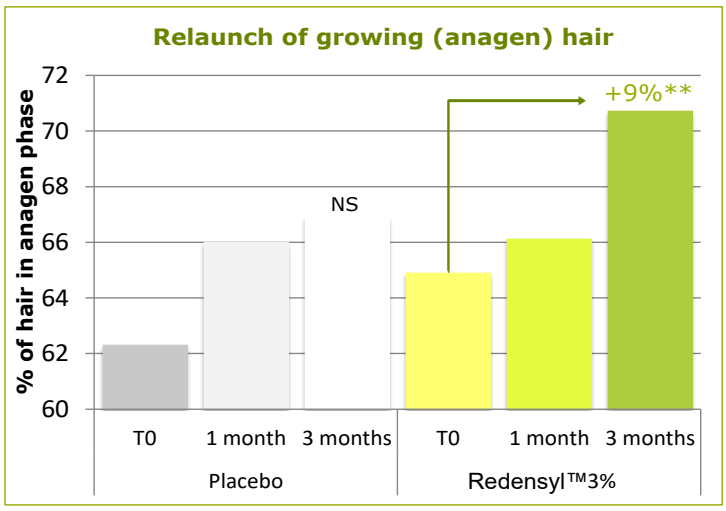
- Shaving of a 1.5 cm^2 area
- Analysis on 0,7 cm^2

Counting of anagen hair (=growing)

PROTOCOL:

Analysis of the volunteers' scalp of the number of hair in anagen phase.

- Slight non significant placebo effect up to D84 (activation of micro-circulation)
- Redensyl™ stimulates up to +9% the number of hair in anagen phase.



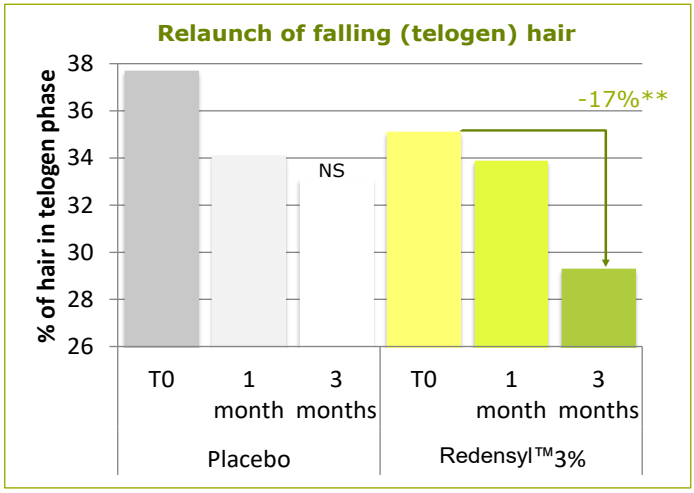
**p<0.01, compared to untreated, Student's t Test

Counting of telogen hair (=falling)

PROTOCOL:

Analysis of the volunteers' scalp of the number of hair in telogen phase.

- Slight non significant placebo effect up to D84 (activation of micro-circulation)
- Redensyl™ reduces down to -17% the number of hair in telogen phase.

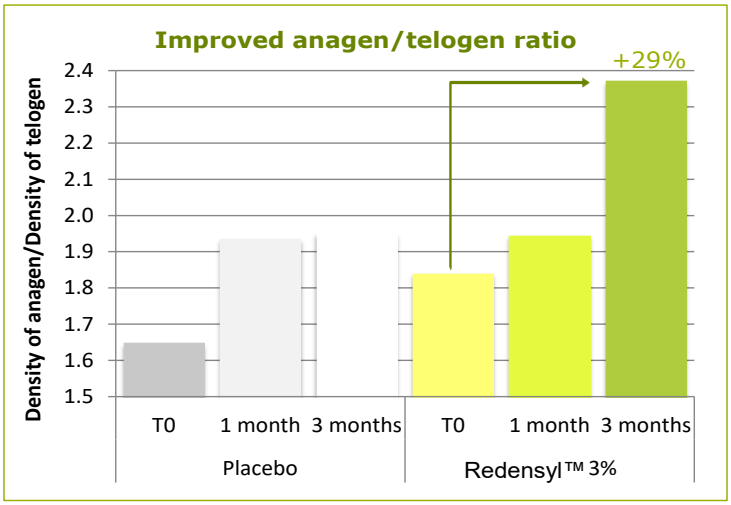


Follow up of the anagen/telogen ratio

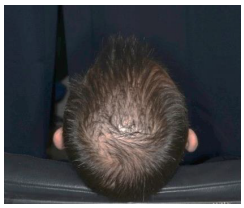
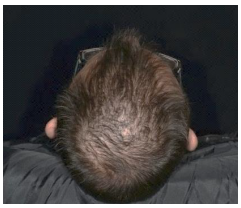
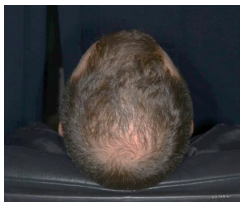
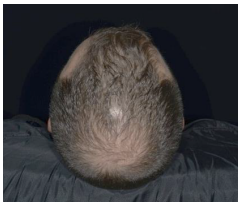
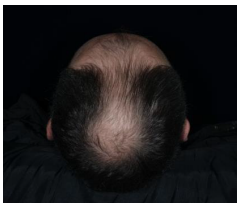
PROTOCOL:

Analysis of the volunteers' scalp of the number of the ratio of anagen versus telogen hair.

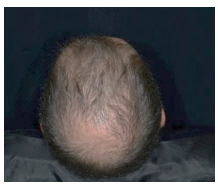
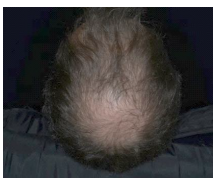
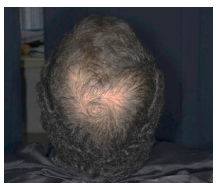
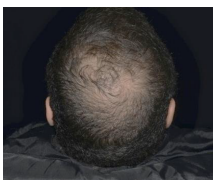
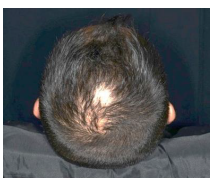
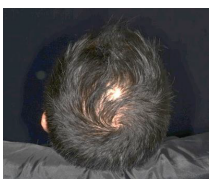
- After 3 months, Redensyl™ improves the ratio of anagen/telogen by +29%, reaching 2.37 from the initial 1.83



Pictures of volunteers

	BEFORE	D84
Increased density 52 years old		
Reduction of the vortex 38 years old		
Reduction of the bald area diameter 42 years old		

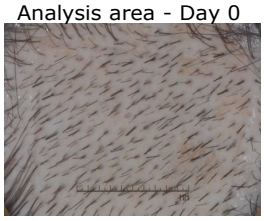
Pictures of volunteers

	BEFORE	D84
Increased density 46 years old		
Reduction of the vortex 36 years old		
Increased density 29 years old		

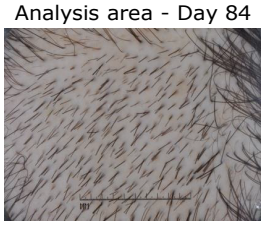
Details – before/after

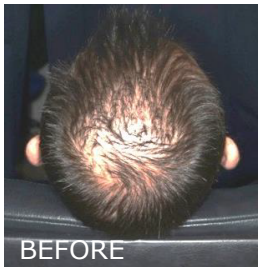
Criteria	#3
Age	**52 years old**
% of new anagen hair	**+ 10.8%**
% of density of hair increase	**+ 17%**
Number of new hairs / cm^2	**+ 47 hairs/ cm^2**
Total number of new hairs on the scalp (600 cm^2)	**+ 28,200 hairs**
Number of new hair per month on the scalp	**+ 9,400 hairs**

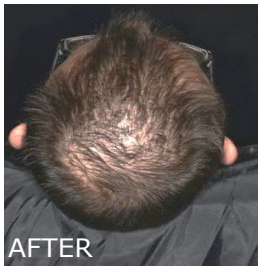
Analysis area - Day 0



Analysis area - Day 84







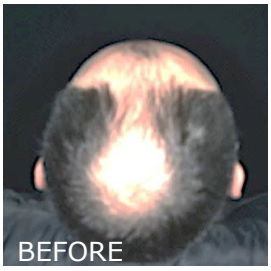
- **Visible redensification of the scalp**

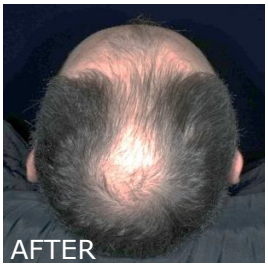
Details – before/after

Criteria	#6
Age	**42 years old**
% of new anagen hair	**+ 19.2%**
% of density of hair increase	**+ 17%**
Number of new hairs / cm^2	**+ 43 hairs / cm^2**
Total number of new hairs on the scalp (600 cm^2)	**+ 25,800 hairs**
Number of new hair per month on the scalp	**+ 8,600 hairs**

Analysis area - Day 0

Analysis area - Day 84

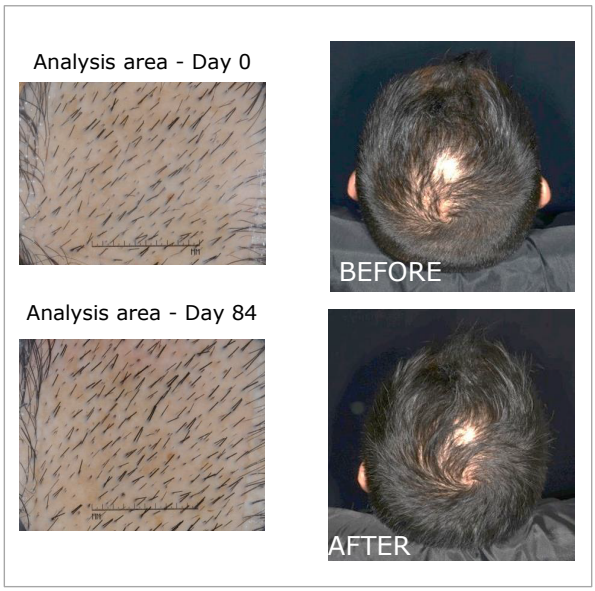




- **Hair loss stopped, a visible increase of hair density**

Details – before/after

Volunteer	#26
Age	**29 years old**
% of new anagen hair	**+ 9.2%**
% of density of hair increase	**+ 17%**
Number of new hairs / cm^2	**+ 29 hairs / cm^2**
Total number of new hairs on the scalp (600 cm^2)	**+ 17,400 hairs**
Number of new hairs per month on the scalp	**+ 5,800 hairs**

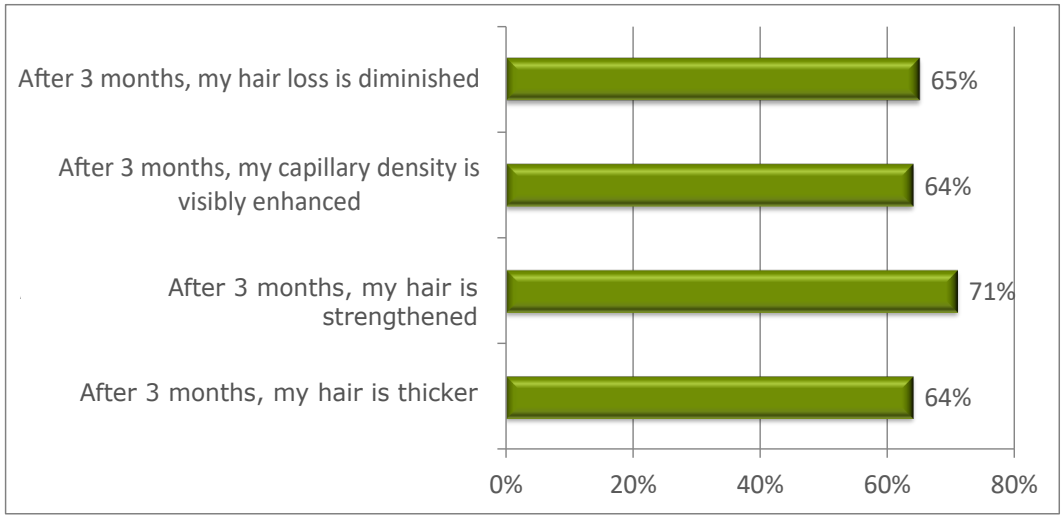


- **Hair looks thicker with a visible improvement of the density**

Self assessment

A self-evaluation run by the volunteers after 84 days.

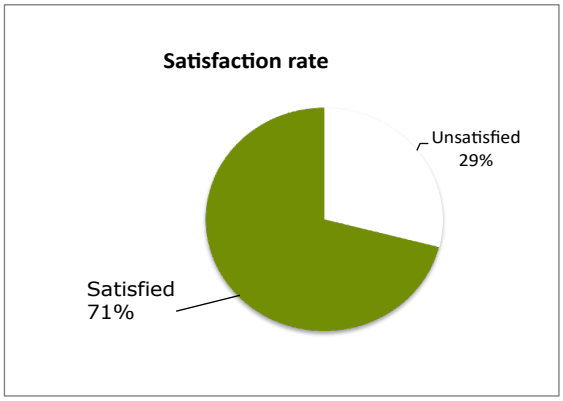
Testers claim to see reduced hair loss, improved capillary density, stronger and thicker hair after three months of treatment.

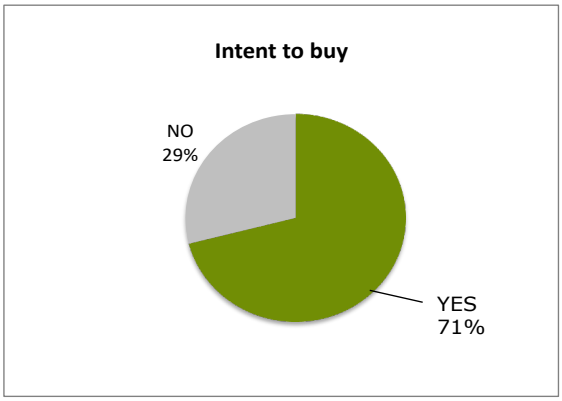


Self assessment

A self-evaluation run by the volunteers after 84 days.

71% of the testers are satisfied by the product, and 71% of them would like to buy the product.





Summary of the clinical assessment

Within 84 days on grade 3 to 4 alopecic volunteers:

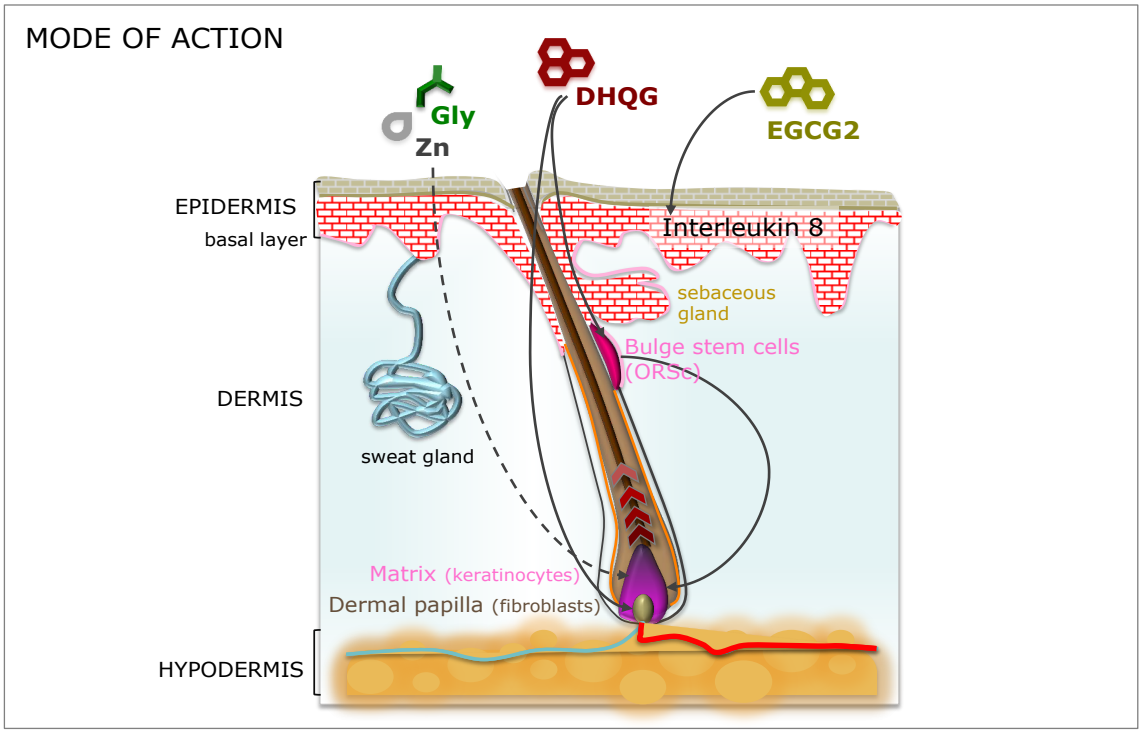
85% of volunteers showed clinical improvements:

- **+9%** of anagen hair
- **-17%** of telogen hair
- **+29%** in the anagen/telogen ratio

An average +8% increase of hair density, corresponding to,

- **+10,000 new hairs** on a total 600 cm^2 scalp surface
- Up to **+28,200 new hairs**

Redensyl™ - the Hair Growth Galvanizer



Targeting existing hair follicle stem cells

1. A reactivation of the bulge stem cells
2. A metabolic boost of dermal papilla cells
3. A shut down of inflammatory reactions
4. Excellent results on grade 3 to 4 alopecic volunteers:
   - Hair are **denser**
   - Hair look **thicker**
   - **Increase** in hair **growth**
   - **Decrease** in hair **loss**
   - A **better ratio anagen/telogen**
   - **Visible results** in 84 days

REDENSYL™

Morgan's Since 1873

Comparison with esthetic surgery

Hair transplantation surgery:

- A hair transplantation surgery enables to make an average of 2016 grafts [1]
- Grade 3 to grade 4 alopecic patients need between 1600 to 2200 hair grafts [2]
- Each graft contains 4 hair [2], so each transplantation gives 6400 to 8800 new hairs
- 65% of the patients undergo a single hair transplantation [1]
- Up to 3 hair grafts sessions can be needed to get the appropriate hair density [1]

Redensyl™ gives better results than one hair transplantation surgery (+10,000 new hairs in average, up to +28,200)

[1] International Society of Hair Restoration Surgery: 2013 Practice Census Results
[2] Bernstein Medical center www.bernsteinmedical.com/hair-transplant/follicular-unit-transplantation/graft-numbers/

Applications

MEN

- Anti hair loss lotion and shampoo
- Hair growth spray
- Anti aging global hair serum
- Shampoo for thin hair
- Preventive hair care shampoo

WOMEN

- Mask, or leave-on hair care products
- Preventive hair care shampoo
- Post trauma hair treatment
- Anti aging global hair serum

- Eyelash growth mascara
- Eyelash growth primer
- Eyebrows redensifier

Focus on the product

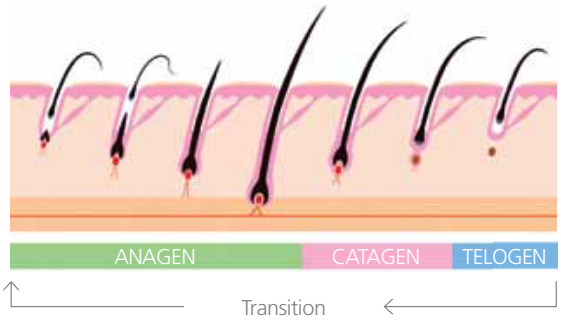
Hair loss in numbers

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

The normal cycle for hair

The hair cycle is made of three phases:

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



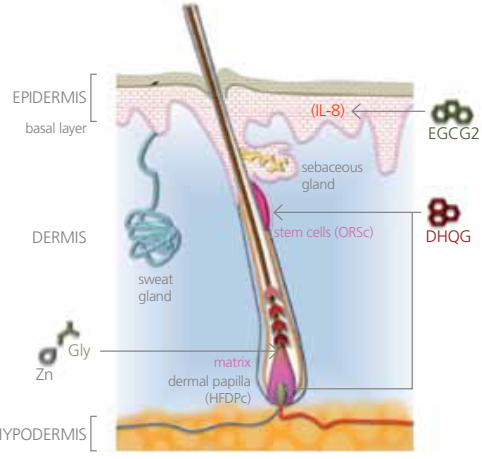
Hair loss and stem cells

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

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

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

- Dihydroquercetin-glucoside (DHQG): a stabilized polyphenol which activates the division of hair follicle stem cells, while maintaining their differentiation properties. It protects stem cells from apoptosis (BCL2 activation), and drives them towards the anagen cycle (β-catenin activation), while boosting the metabolism of dermal papilla fibroblasts.
- EGCG-glucoside (EGCG2): a stabilized EGCG derivative used to reduce the typical inflammatory state of alopecic scalp (reduction of IL-8), and capture free radicals[1].
- Glycine: a major constituent of hair proteins, mainly keratin associated proteins (KAP), which favors hair growth[2].
- Zinc: a very important co-factor for numerous enzymes, favoring the incorporation of cystin in keratin for a stronger hair shaft[3].



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

1. Source: Chem Phys Lipids. 2000 Jun ; 106(1):53-63. 2. Source: J Invest Dermatol. 1994 Sep;103(3):310-7. 3. Source: J Nutr. 1971 Apr;101(4):445-52.

Biological activity

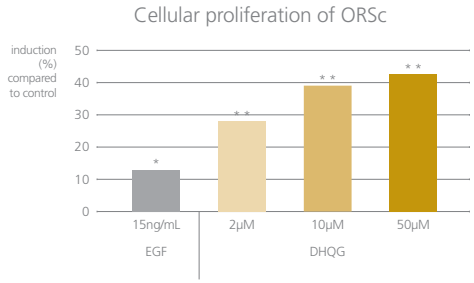
Four actions on ORSc stem cells (in vitro tests)

1. Stimulating ORSc proliferation:

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

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

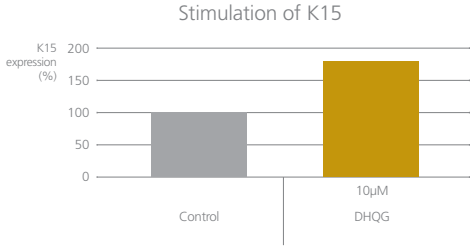
*p<0.01, **p<0.001 compared to control, Student's t-test



2. Maintaining their stem cell's phenotype:

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

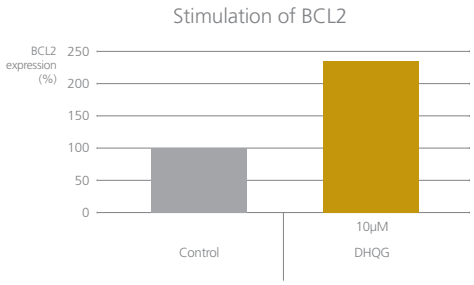
Result: DHQG at 10µM multiples by almost 2 times the mRNA synthesis of K15, a qualification marker of stem cell's phenotype.



3. Avoiding apoptosis:

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

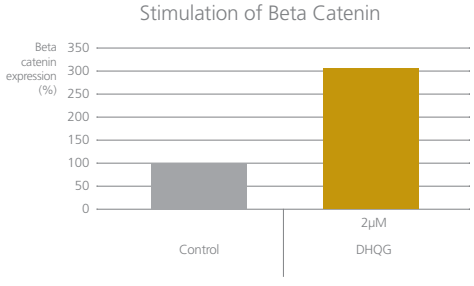
Result: DHQG at 10µM increases by 2 times the mRNA synthesis of BCL2, showing the anti-apoptosis effect of this molecule.



4. Activating differentiation:

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

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



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

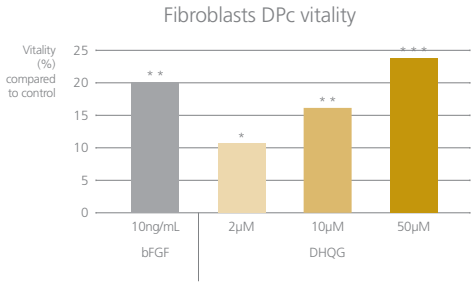
Biological activity

Increase of Fibroblasts DPc vitality (in vitro tests)

Human fibroblasts dermal papilla cells (HFDPc) were incubated for 48 hours in a basal medium and treated with increasing doses of DHQG (the major component of Redensyl®) or bFGF as a reference.
Their metabolic activity was evaluated thanks to a XTT reduction assay.

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

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

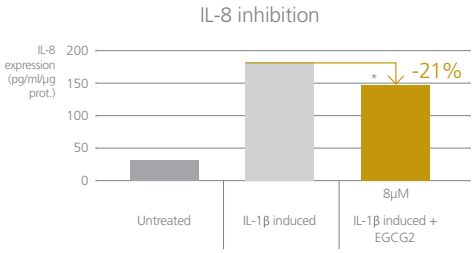


Decrease of skin irritation (in vitro tests)

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

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

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

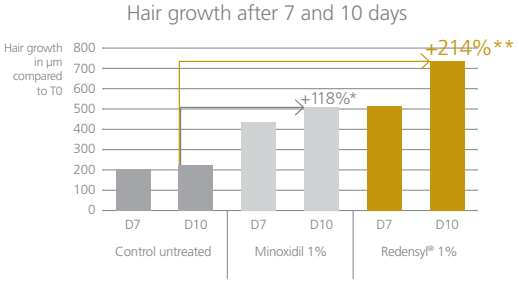


Increase of hair follicle length (ex vivo Philpott test)

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

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

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

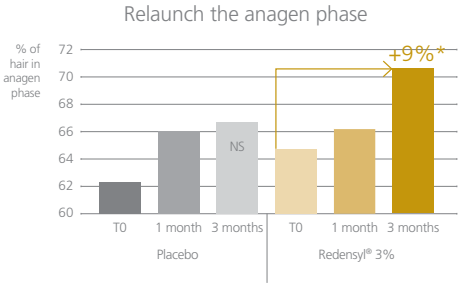


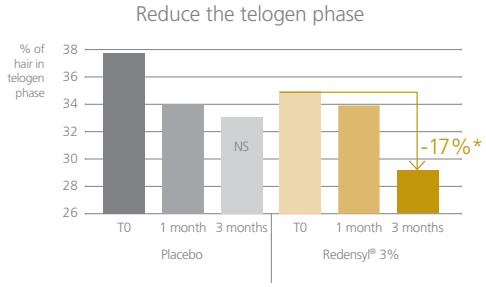
Visible increase of hair follicle size

Efficacy

Reactivate the hair growth cycle (clinical evaluation)

The efficiency of Redensyl® at 3% was evaluated in a double-blind test versus a placebo. Twenty six male volunteers were selected by following specific inclusion criteria: between 18 to 70 years old, brown to dark hair, with a minimum density of hair of 150 hair/cm² and 40 telogen hair/cm², with clinically confirmed grade 3 to 4 alopecia.
Volunteers applied the placebo or the product with 3% of Redensyl® on their whole scalp daily for 3 months.
A shaved area of 1.5cm² was defined on each volunteer to allow the measurements on a window of 0.7cm² at D0, D28 and D84.
Phototrichograms were realized using a NIKON camera associated with Canfield® Epiflash System and a contact plate to press hair on the scalp. Analysis were run with Photoshop CS5 extended® and permitted to define if hair were in anagen, telogen or undetermined phase.





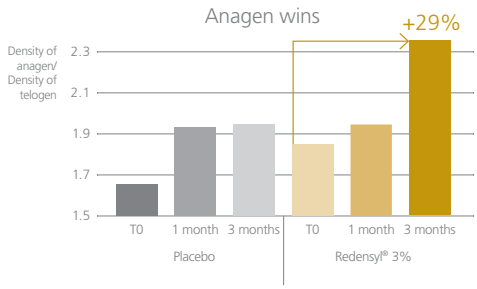
*p<0.01 compared to untreated, Student's t-test

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

Rebalance the anagen/telogen ratio (clinical evaluation)

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

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



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

Efficacy

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

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

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

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

Macro pictures (Phototrichograms)

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

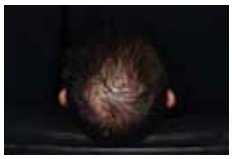
J0

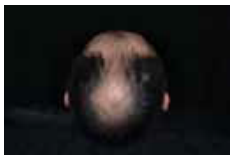
3 months

Scalp pictures

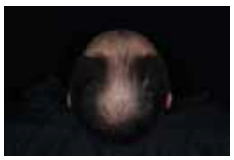
Results: Hair loss stopped, a visible increase of hair density is noticeable.

Before





After



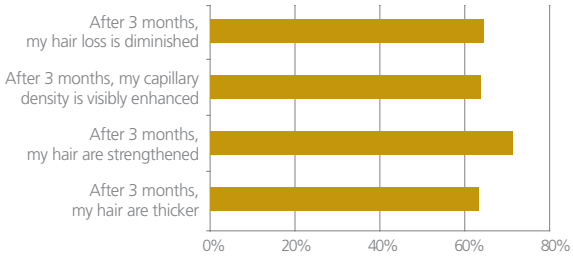
REDENSYL™

Summary

Self-evaluation of Redensyl® (clinical)

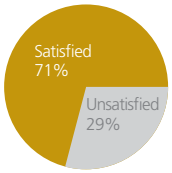
A self-evaluation after 3 months was run by the volunteers.

Results: Testers claim Redensyl® at 3% reduced their hair loss, improved the capillary density by strengthening and thickening their hair after three months of treatment.

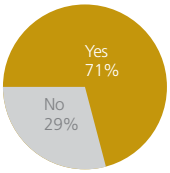


71% of the testers are satisfied by the product, and 71% of them would like to buy the product.

+10,200 hair in average in 3 months: better results than one hair transplantation procedure [1].



Satisfaction rate



Purchase intension

Technical information

Suggested INCI:	Water, Glycerin, Sodium Metabisulfite, Glycine, Larix Europaea Wood Extract, Zinc Chloride, Camellia Sinensis Leaf Extract
Origin:	Plant extracts and Biotechnology
Preservation:	Preservative-free
Appearance:	Clear, yellow liquid
Solubility:	Water soluble
Dosage:	1-3%
Processing:	Can be added at the end of the formulation process under stirring or homogenizing or can be heated for a short time with the water phase of formulation. Formulate at temperature below 50°C.

Claims

Claims:	Anti-hair loss, stimulation of hair growth, re-densification of hair on scalp, stimulation of eyelash growth, activation of eyebrow growth.
Applications:	Anti-hair loss treatment, hair lotion, hair serum, anti-aging hair serum, eyelash growth serum, active mascara, eyebrow enhancers.

1. Source: International Society of Hair Restoration Surgery - 2013 Practice Census Statistics – 2,016 of grafts per session, 4 hair by graft, apprx. 8,100 hair in one session

ANAGAIN™

Morgan's Since 1873

AnaGain™
Stimulating hair growth and fighting hair loss

An Organic Pea Sprout Extract to Rebalance the Hair Life Cycle
Based on sprouts of organic pea, AnaGain™ reduces hair loss by inducing dermal papilla cells to reactivate hair growth.

Hair loss affects both women and men. It is caused by an imbalance of the hair growth cycle leading to a reduced number of growing (anagen) hair combined with an in - creased number of degenerating (telogen) ones.

AnaGain™ was shown, thanks to DNA microarray analysis of plucked hair follicles, to activate, in the dermal papilla, specific signal molecules which are required to initiate the growth of a new hair.

A clinical study conducted for three months on volunteers with mild to moderate hair loss showed the capacity of AnaGain™ to reduce hair loss:
- the density of anagen hair was increased by about 8 %
- the density of telogen hair was reduced by more than 28 %.

As a consequence, AnaGain™ increased the hair growth coefficient (proportion of active hair follicles) from 4 to 7.2 indicating a strong hair-regrowing effect.

By reactivating hair growth, AnaGain™ helps the hairs to keep their original density and thickness.

AnaGain™ is COSMOS approved*.

AnaGain™
- Stimulates hair growth at the root
- Prolongs the life cycle of hair
- Fully restores the vitality of the hair
- For denser hair in just 3 months

Applications
- Anti-hair loss, hair-regrowth formulations
- Anti-aging hair care products
- Tonics, serums, conditioners, masks, shampoos

Formulating with AnaGain™
- Recommended use level: 2–4 %
- Incorporation: For cold processes, dissolve AnaGain™ into the aqueous phase. In cold / hot processes, add during the cooling phase below 60 °C.
- Thermostability: Temperatures of up to 60 °C for a short time do not affect the stability of AnaGain™.

INCI (EU/ PCPC) Declaration
AnaGain™ (standard version):
Pisum Sativum (Pea) Sprout Extract (and) Phenoxyethanol (and) Sodium Benzoate (and) Aqua/ Water

AnaGain™ pf (preservative-free version, COSMOS approved * version):
Pisum Sativum (Pea) Sprout Extract (and) Alcohol (and) Aqua / Water

AnaGain™ pwd (powder version, 2-fold concentrated, COSMOS approved * version):
Pisum Sativum (Pea) Sprout Extract (and) Isomalt (and) Aqua / Water

* Raw material approved by ECOCERTGREENLIFE in accordance with the COSMOS Standard

The Hair Matrix
The most active part of the hair

The Dermal Papilla Controls Hair Follicle Development and Growth

Located in the deepest part of the hair bulb, the hair matrix is one of the most rapidly proliferating tissues in the human body.

The hair matrix, which is a part of the epidermis layer containing keratinocytes, embeds a “ball” of specialized dermal cells called dermal papilla (DP).

The DP plays a major role in hair follicle development and growth: it initiates the growth of a new hair by:

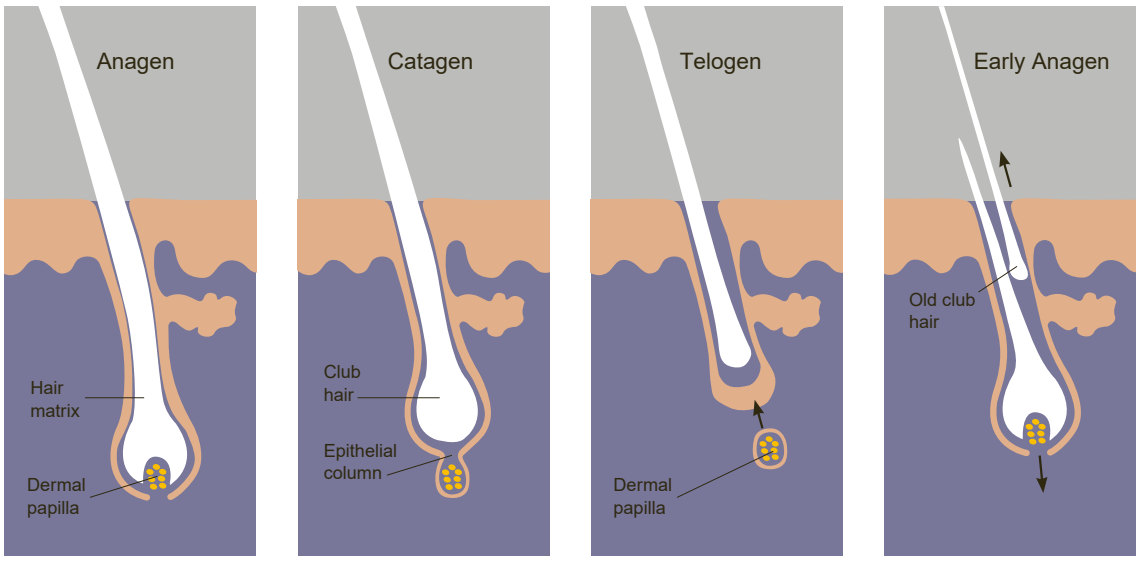
- controlling the switch from degeneration (telogen) to growth (anagen) phase in the hair life cycle
- instructing the surrounding epithelial cells (the hair matrix) to proliferate, move upward and differentiate into the multiple cell types which will constitute the outgrowing hair shaft as well as its root sheaths.

The Hair Growth Cycle

Hair follicles undergo cyclical and asynchronous growth. This cycle is made up of 3 phases (anagen, catagen and telogen); each hair passes through the phases independently of the neighboring hairs.

- During the anagen (growing) phase which lasts 3 to 5 years, the DP initiates the creation of a new matrix which will lead to the formation of a new hair.
- Then the hair moves to the regression (catagen) stage for about 3 weeks. During this transition period, the hair bulb separates from the DP, and the hair follicle shrinks and migrates towards the scalp surface. The DP remains intact and is pulled or migrates upwards.
- At the end of the telogen (resting) phase which lasts up to 4 months, the hair follicle reenters the anagen phase: the DP and the base of the follicle join together again and a new hair begins to form. If the old hair has not already been shed, the new hair pushes the old one out and the growth cycle starts all over again.

The Hair Growth Cycle



ANAGAIN™

Morgan's Since 1873

Hair Loss
Is linked to an imbalanced hair growth cycle

Hair Loss Has Several Causes
In people with healthy hair, about 85 –90 % of the hair is in the anagen phase and the other 10 –15 % is in the telogen one.

Hair loss, also called alopecia, is caused by an imbalance of the hair growth cycle which results from several factors (androgen metabolism, genetics and stress).
It is characterized by:

- changes in the proportions of anagen and telogen hair: the number of anagen hairs is reduced and at the same time too many hairs remain in the telogen phase.
- a decrease in the duration of anagen phase leading to shorter and thinner hair
- a prolongation of the interval separating the loss of a hair in telogen phase and the emergence of a replace - ment anagen hair.

Women and Men are Affected but in Different Ways
Hair loss affects at least 50% of men and about 25 % of women by the age of 50.
40 % of women aged 70 and over are concerned.

Besides, women experience diffuse hair loss and tend to lose the hair on the top of their head. Hair loss in men may be much more extensive, affecting mostly the temporal areas and the top of the head.

AnaGain™

A pea sprout extract which rebalances the hair growth cycle

AnaGain™ is based on Organic Pea Sprouts
The pea (Pisum sativum) is a vegetable with pod fruits. Each pod contains several peas that are rich in proteins, starch and fibers.

Sprouts from organic pea were selected as a source of AnaGain™ because of their richness in phytonutrients. These “health promoting phytochemicals” protect the plant from disease, damage, pathogens, extreme UV, pollutants and help to defend it against herbivores. Besides, many of these phytochemicals are known to exert beneficial effects on human health. Phytonutrients are highly abundant in sprouts because at this stage plants are not yet lignified and thus, especially vulnera - ble. This is why sprouts are the plant material with the highest level of phytonutrients.

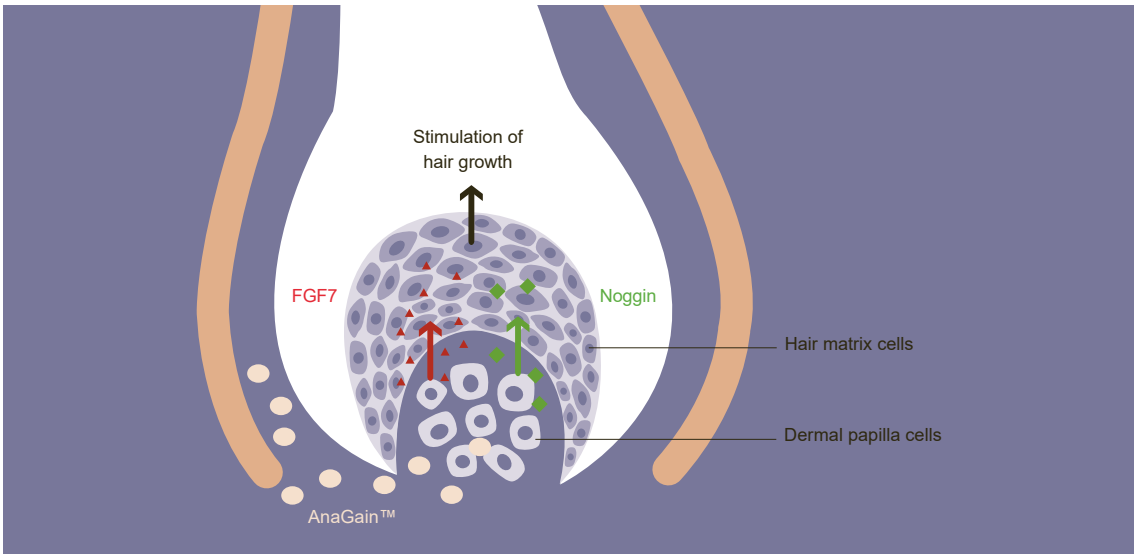
An Environmentally-Friendly Process
Pea sprouts are produced indoors without soil.
- Organic pea seeds are first soaked in water then transferred to rotating containers that provide drainage, light, aeration and agitation.
- After a few days of incubation in the containers, the sprouts are harvested and then extracted with water and purified.

This technique has many advantages:
- availability of plant material independent of the season, soil conditions and market demand
- plant material completely free of environmental pollutants and pesticides
- low water requirements.

AnaGain™ Activates the Dermal Papilla to Induce Hair Growth
AnaGain™ was shown, thanks to the DNA microarray technique conducted on plucked hair follicles, to stimulate, in the DP, specific signaling molecules which are required to initiate the growth of a new hair:
- Noggin, a protein that shortens the telogen phase
- FGF-7, fibroblast growth factor-7, which promotes the proliferation activity of the matrix keratinocytes to start a new anagen phase.

These results were confirmed with the phototrichogram technique: After three months’ treatment, AnaGain™ was found to reduce hair loss and to increase hair vital- ity: the density of anagen hair was increased whereas the density of telogen hair was strongly reduced.

Mechanism of AnaGain™



AnaGain™
Study results

Effect on Hair Gene Expression in Volunteers from 46 –60

The effect of AnaGain™ on hair growth was evaluated using DNA microarray technology. This test was conducted on hair bulbs plucked from the occipital area of the head of 10 volunteers (4 women and 6 men aged from 46 to 60 – mean: 53.9). Hairs were pulled out before and after a 14 day treatment with a gel con - taining 2 % AnaGain™.

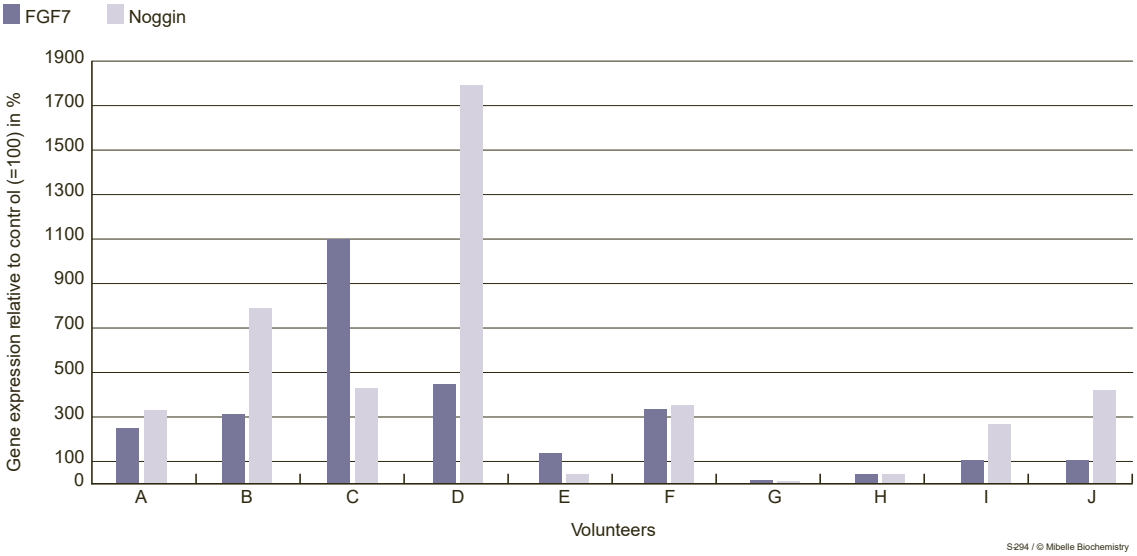
The expression of genes important in hair physiology was analyzed by quantitative PCR.

Gene expression analysis conducted on plucked hair bulbs after a 2 week treatment with 2 % AnaGain™ showed an up-regulation of two DP signaling molecules required to initiate a new hair follicle growth cycle:

- the expression of noggin, a protein that shortens the telogen phase, was increased by 85 % on average
- the expression of FGF-7 (fibroblast growth factor-7), which promotes the proliferation activity of the matrix keratinocytes at the beginning of a new anagen phase, was increased by 56% on average.

These results showed that AnaGain™ can stimulate the DP to induce the growth of a new hair.

Effect on the Expression of DP Signaling Molecules



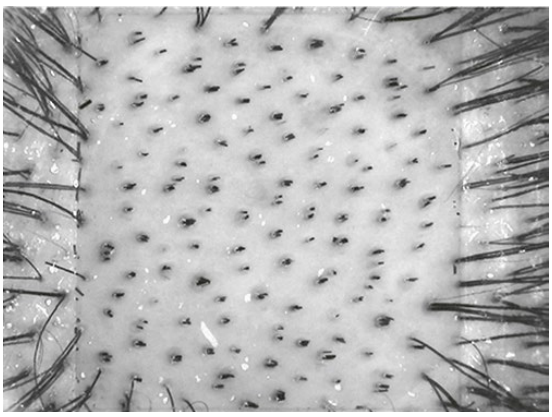
AnaGain™
Study results

Anti-Hair Loss Effect and Hair Growth Reactivation

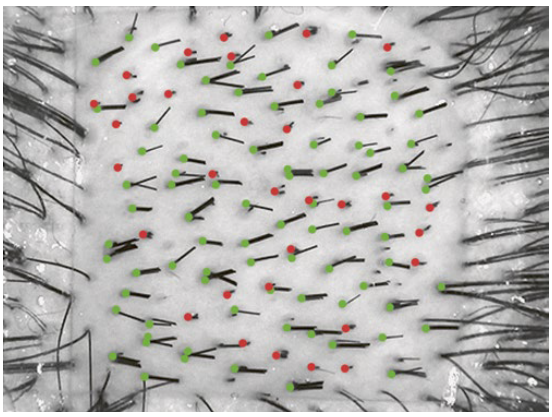
The effects of AnaGain™ on the hair growth cycle were evaluated using the phototrichogram technique on 20 volunteers suffering from mild to moderate hair loss corresponding to telogen hair superior or equal to 15 % for women and 20 % for men. 17 women and 3 men aged from 21 to 37 (mean: 26) applied a gel containing 4 % AnaGain™ to their scalps twice a day for three months.

The phototrichogram is an non-invasive technique which allows measurements of the proportion and the density of hair in the different phases of the hair growth cycle. For this, an area of 0.7 cm^2 was defined in the scalp (vertex area). The hairs in this area were cut short, a photograph was taken at this moment and then again 2 days later. Hairs that started to grow during these 2 days are in the anagen phase and hairs that stopped growing are in the telogen phase.

Phototrichogram Technique



Anagen hair Telogen hair



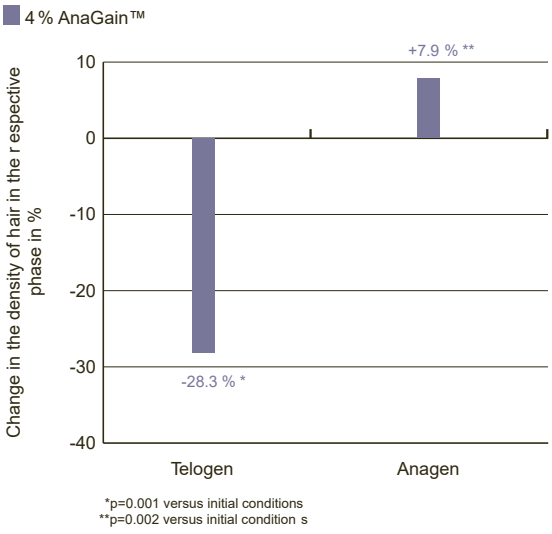
Morgan's Since 1873

Results showed that AnaGain™ significantly:
- decreased the density of telogen hair (–28.3 % / p = 0.001 versus initial conditions)
- increased the density of anagen hair (+7.9 % – p = 0.002 versus initial conditions).

AnaGain™ can thus reduce hair loss which is characterized by too much telogen hairs and reduced anagen ones.

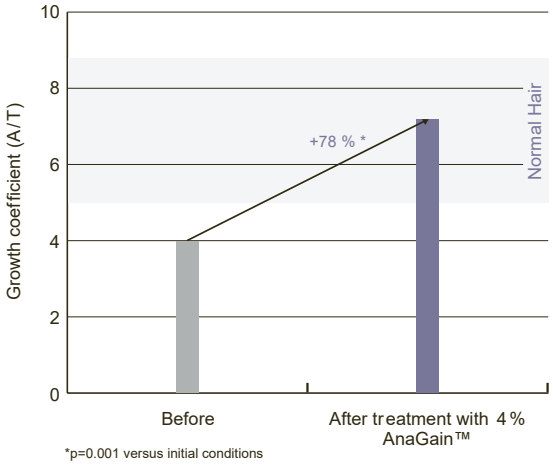
As a consequence, with AnaGain™, the hair growth coefficient (A / T ratio) was significantly increased. The ratio of the number of anagen hairs to the number of telogen hairs indicates the proportion of active hair follicles. If A / T is above 5, the hair loss is normal. After three months' treatment with 4 % AnaGain™, the A / T ratio improved from 4 to 7.2 thus going clearly beyond 5. This indicates that after treatment with AnaGain™, hair regeneration is restored to a normal level.

Reduction of Hair Loss / Stimulation of Hair Growth



*p=0.001 versus initial conditions
**p=0.002 versus initial condition s

Stimulation of the Hair Growth Coefficient



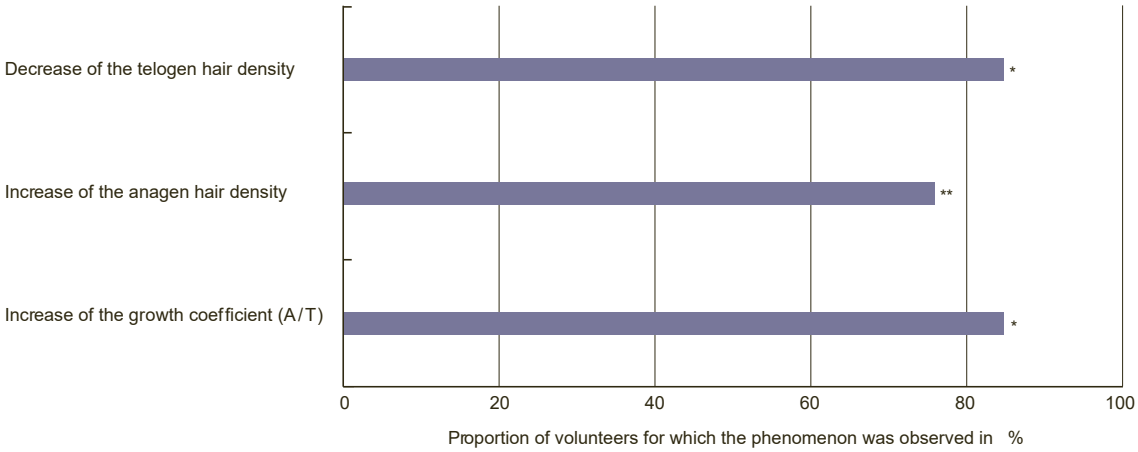
*p=0.001 versus initial conditions

AnaGain™
Study results

The anti-hair loss effect of AnaGain™ was observed on a very large part of the panel:

- the decrease of the density of hair in the telogen phase was observed in 85% of the volunteers
- the increase of the density of hair in the anagen phase was observed in 75% of the volunteers
- the increase of the growth coefficient was observed in 85% of the volunteers.

Anti-Hair Loss Effect Observed on a Large Part of the Panel



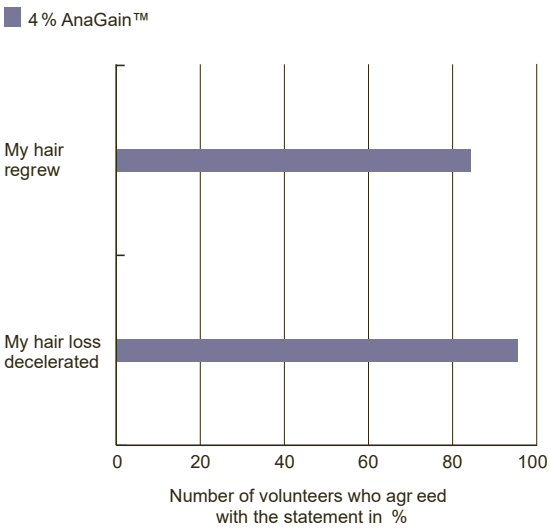
*p=0.001 versus initial conditions
**p=0.002 versus initial condition s

Perception of the Efficacy by Self-Evaluation
At the end of the study, the volunteers were asked, using a questionnaire, to tell whether they perceived improvements of specific criteria.

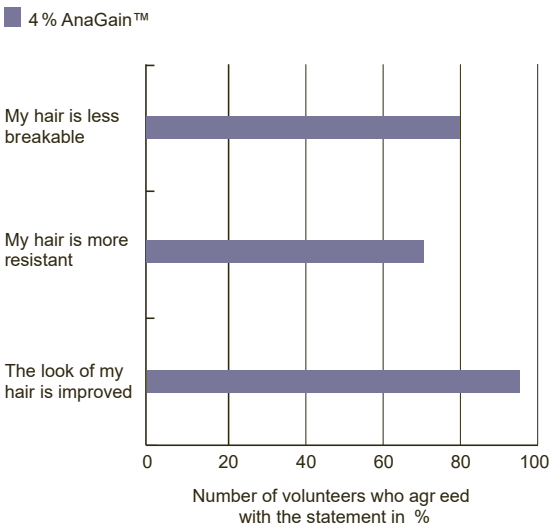
Results showed that, after 3 months' treatment with AnaGain™:

- 85 % of the volunteers noticed a slight to strong regrowth of their hair
- 95 % of the volunteers noticed a slight to strong deceleration of their hair loss
- 80 % of the volunteers found their hair less breakable
- 70 % of the volunteers found their hair more resistant
- 95 % of the volunteers noticed a slight to strong improvement in the look of their hair.

Perception of the Anti-Hair Loss Effect



Perception of an Improved Hair Quality



ANAGAIN™

Morgan's Since 1873

AnaGain™
Stimulating hair growth and fighting hair loss

AnaGain™
- Stimulates hair growth at the root
- Prolongs the life cycle of hair
- Fully restores the vitality of the hair
- For denser hair in just 3 months

Applications
- Anti-hair loss, hair-regrowth formulations
- Anti-aging hair care products
- Tonics, serums, conditioners, masks, shampoos

Marketing Benefits
- In vivo proven on women and men
- Organic source of the plant
- Advanced Ingredient Award Winner
- Available in COSMOS approved versions

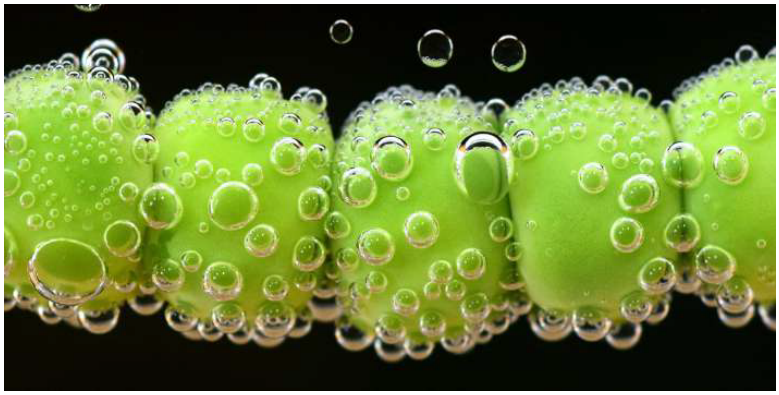
COSMOS APPROVED

Innovating for your success

Mibelle Biochemistry designs and develops innovative, high-quality actives based on naturally derived compounds and profound scientific know-how. Inspired by nature – Realized by science.

Mibelle AG Biochemistry, 5033 Buchs/ Switzerland, Phone +41 62 836 17 31, info@mibellebiochemistry.com, www.mibellebiochemistry.com

ACB Pisum Sativum Peptide



BACKGROUND

Hydrolyzed proteins such as soy, wheat or oat have been used to impart conditioning benefits and film-forming properties to the hair for decades. These hydrolysates are comprised of random amino acid sequences that aid in improving the elasticity, texture, and hydration of the hair. Recent efforts within the Nutritional Industry have focused on the selection of more precise protein fragments to improve the benefits of supplements. In the course of this research, it has become clear that protein fragments from different sources have varied benefits. To use the verbiage of Malcolm Gladwell, one of the "Outliers" is *Pisum sativum*.

Recently, *Pisum sativum* proteins have attracted the interest of nutrition and health advocates as a plant-based, hypoallergenic protein that yields a high Biological Value (BV). Biological Value is an accurate indicator of the available nutritional potential of a protein. On average, *Pisum sativum* Protein has a 65.4% BV, in comparison to soy protein which only has a 50.0% BV average and wheat protein with only a 49.0% BV average. While it may have had a modest beginning, the enhanced bioavailability of *Pisum sativum* proteins has caught the market by storm as the quality alternative to other vegetable proteins; providing benefits such as high solubility (for easy digestion), enhanced kidney function, and lowering of the blood pressure.

SCIENCE

Proteins are traditionally hydrolyzed using acids, alkalis, and enzymes or some combination there of to produce random amino acid sequences. While traditional methods of hydrolysis are well accepted and effective, they are simplistic efforts to duplicate normal cellular protein catabolism whereby cells digest proteins into specific sequences to meet their nutritional needs. Active Concepts has harnessed the digestive abilities of a proprietary non-GMO bacterial strain, *Lactobacillus bulgaricus,* to produce *Pisum sativum* peptides with a controlled molecular weight of approximately 750 Da.

Pisum sativum protein is a complete source of Essential Amino Acids (EFAs). In fact, *Pisum sativum* has the most balanced amino acid profile of any vegetable protein, consisting of 22 amino acids, notably, rich in lysine[2]. Lysine functions as a vital building block in human biology. Since lysine synthesis does not occur in the body naturally it must be obtained from outside sources, such as protein derived from *Pisum sativum*.

Code Number: 16810

INCI Name: Pisum Sativum (Pea) Peptide
INCI Status: Conforms
REACH Status: Complies
CAS Number: 90082-41-0
EINECS Number: 290-130-6
Origin: Botanical
Processing:
- GMO Free
- No Ethoxylation
- No Irradiation
- No Sulphonation

Additives:
- Natural Antimicrobial: Leuconostoc/ Radish Root Ferment Filtrate
- Preservatives: None
- Antioxidants: None
- Other additives: None

Solvents Used: Water
Appearance: Clear to Slightly Hazy Liquid
Soluble/ Miscible: Water Soluble
Ecological Information:
- 87.30% Biodegradability

Microbial Count:
- < 100 CFU/g, No Pathogens

Suggested Use Levels: 1.0 – 5.0%
Suggested Applications: Hair & Skin Care, Anti-aging, Antioxidant, Hydrating, Smoothing, Volumizing

ACB Pisum Sativum Peptide

BENEFITS

Anti-Aging is the latest trend in Hair Care. ACB Pisum Sativum Peptide provides a potent and cost effective solution by delivering volume and antioxidant protection offsetting the symptoms of hair aging. ACB Pisum Sativum Peptide's film-forming properties render it an effective material for hydrating the hair for a silky feel. Recent demand for anti-aging hair products has prompted formulators to seek out materials and manufacturing methods that will allow targeted claims. ACB Pisum Sativum Peptide reduces the damage caused by free radicals to promote the scalp and follicle health essential producing youthful, voluminous looking hair.

EFFICACY

A series of *in-vivo* and *ex-vivo* studies were performed on volunteers and human hair tresses to evaluate the ability of ACB Pisum Sativum Peptide to provide perceivable benefits to the hair.

The first study study was conducted at Gaston College Technology Center (USA) where the diameter of colored hair was measured at different intervals to determine an increase in hair thickness. Using 60 strands of hair, a 2.0% solution of ACB Pisum Sativum Peptide was applied to each strand. A solution of 2.0% Wheat Hydrolysate in water was used as a positive control for comparison. Immediate results showed an average increase in hair diameter of 14.08% when using the ACB Pisum Sativum Peptide. Four hours after application an average increase of 13.65% was measured when compering the ACB Pisum Sativum Peptide to the control. These results indicate that 2.0% ACB Pisum Sativum Peptide provides thickening benefits to the hair.

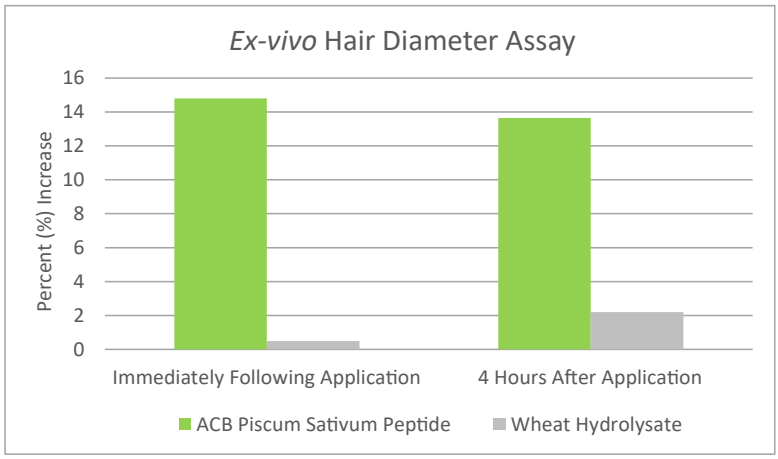


Figure 1. Increase in hair diameter after application of 2.0% ACB Pisum Sativum Peptide in solution compared to the contol of 2.0% Wheat Hydrolysate in solution

Microscopy Imaging of the individual strands were then taken to visually demonstrate the increase in hair diameter achieved when using 2.0% ACB Pisum Sativum Peptide in comparison to 2.0% Wheat Hydrolysate. From these images it can be seen that the ACB Pisum Sativum Peptide is instantly substantive to the hair producing an even film, whereas the Wheat Hydrolysate beads onto the strand. These images further demonstrate the increase in hair diameter achieved when using ACB Pisum Sativum Peptide compared to the Wheat Hydrolysate. ACB Pisum Sativum Peptide is able to effectively thicken the strands for fuller and younger looking hair giving a revolutionary step for anti-aging hair care products.

ACB Pisum Sativum Peptide

Figure 2. Individual strand following immediate treatment with 2.0% Wheat Hydrolysate

Figure 3. Individual strand following immediately treatment with 2.0% ACB Pisum Sativum Peptide

Figure 4. Individual strand four hours after treatment with 2.0% Wheat Hydrolysate

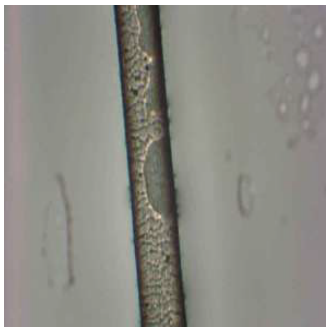


Figure 5. Individual strand four hours after treatment with 2.0% ACB Pisum Sativum Peptide

Increased hydration of the hair is a key benefit of hydrolyzed proteins. As evidenced in an *in-vivo* study, ten (M/F) subjects between the ages of 24 and 37 were instructed to apply either an untreated control, a solution containing 5.0% ACB Pisum Sativum Peptide, or a 5.0% solution containing Wheat Hydrolysate to their hair as a leave-in conditioner, once a day for a week. A DPM 9003 Nova Impedence Meter was used to test the moisture levels on the hair. The results demonstrated a comparable increase in hair hydration on subjects using both a 5.0% solution of ACB Pisum Sativum Peptide and a 5.0% solution of Wheat Hydrolysate.

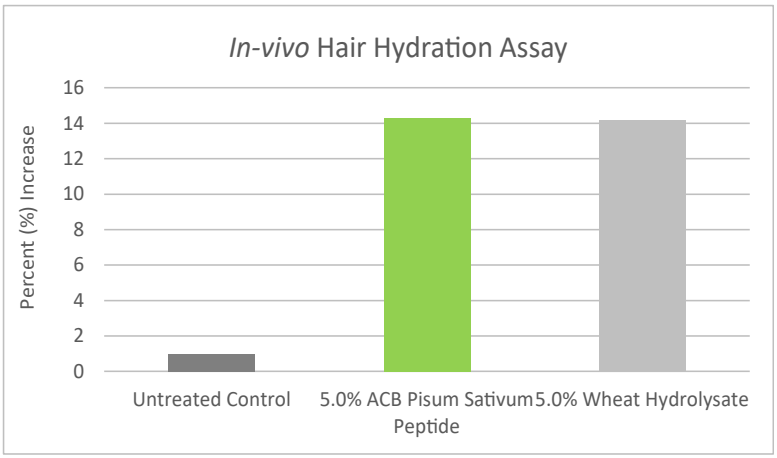


Figure 6. Increase in hair hydration when treated with 5.0% of ACB Pisum Sativum Peptide in solution compared to the contol of 5.0% Wheat Hydrolysate in Solution

ACB Pisum Sativum Peptide

An *in-vivo* half head study was conducted using five participants with a variety of hair types to determine the comparison of using a shampoo and conditioner incorporating 2.0% ACB Pisum Sativum Peptide vs. a control shampoo and conditioner. Each volunteer's hair was photographed before and after washing and blow dry styling with the test and control products. The images of the half head study were used in conjunction with a sensory assessment subjectively rating shine, volume, dry and wet combability, thickness, smoothness, hydration, softness and manageability.

Figure 7. Half-head study to compare hair washed and styled after using a base shampoo and conditioner (left) vs hair washed and styled using a base shampoo and conditioner plus 2.0% ACB Pisum Sativum Peptide (right)

Figure 7 shows that the hair treated with 2.0% ACB Pisum Sativum Peptide appears more voluminous, shiny, soft and healthy than when using the base shampoo and conditioner on their own. Consequently, these results highlight that ACB Pisum Sativum Peptide is capable of enhancing the volume and overall health of the hair perfect for use in anti-aging hair care product lines.

Hair Pollution Protection Assay Analysis

info@activeconceptsllc.com • Phone: +1-704-276-7100 • Fax: +1-704-276-7101

Tradename: ACB Pisum Sativum Peptide

Code: 16810

CAS #: 90082-41-0

Test Request Form #: 3363

Lot #: 48222

Sponsor: *Active Concepts, LLC; 107 Technology Drive Lincolnton, NC 28092*
Study Director: *Maureen Danaher*
Principle Investigator: *Jennifer Goodman*

Test Performed:
Hair Pollution Protection Assay

Introduction

The deleterious effects of pollution in skin and hair care has become a new frontier for anti-aging active ingredients. Environmental pollutants are results of automobile exhaust gas, industrial emissions, and even emissions from simple household chores such as cooking and cleaning. Hair is subject to these environmental aggressions as well as UV irradiation and, unlike the skin, hair is quite vulnerable and lacks self-protection mechanisms. Exposure to environmental pollution can result in dry, brittle hair with decreased strength and elasticity.

Our hair pollution protection assay was conducted to assess the ability of **ACB Pisum Sativum Peptide** to protect the hair from the oxidative effects of air pollution. Hair swatches were treated and exposed to cigarette smoke, and peroxidation of hair lipids were assessed using a Malonaldehyde (MDA) Assay. Pollutant cigarette smoke is a suitable substance containing all key pollution components such as reactive oxygen species (ROS), reactive nitrogen species, and electrophilic aldehydes. Reactive oxidants as well as free radicals from cigarette smoke are closely associated with oxidative stress and secondary oxidative events, such as lipid peroxidation.

The Malondialdehyde (MDA) assay is useful for quantitatively measuring the end product of lipid peroxidation and determining oxidative stress. MDA is frequently used as a bio marker for oxidative stress and, in this case, lipid peroxidation (the breaking down of lipids) due to environmental stress. An increase in MDA indicates an increase in lipid peroxidation and oxidative stress.

Hair Hydration Comparison Assay

info@activeconceptsllc.com • Phone: +1-704-276-7100 • Fax: +1-704-276-7101

Tradename: ACB Pisum Sativum Peptide

Code: 16810

Lot #: NC180315-F

CAS #: 100209-45-8

Test Request Form #: 4642

Sponsor: *Active Concepts, LLC; 107 Technology Drive Lincolnton, NC 28092*
Study Director: *Maureen Danaher*
Principle Investigator: *Parisa Mehrzadeh*

Test Performed:
Gravimetric Analysis of Hair Hydration

Introduction

The study was conducted to evaluate the hair hydration benefits of **ACB Pisum Sativum Peptide** by gravimetric means.

Materials

A. Equipment: Sealed glass chamber, Relative humidly monitor, Analytical balance (Mettler Toledo Model ME4002E). This study was conducted using Sensationnel Bare & Natural Brazilian 100% Virgin Remi Unprocessed Human Hair (Hair Zone Moonachie, NJ).

Methods

Gravimetric analysis is an analytical method in which the analytical signal is a measurement of mass or a change in mass. Substantivity of a material can be measured as a change in mass after the material is exposed to controlled humidity. An increase in hydration can be measured by comparing the weight of the test material at over time after application and signifies hydrating capabilities.

Before measuring the moisturizing effect, the hair swatches were kept in a humidity controlled box (22°C, 50% Relative Humidity) for 24 hours. Hair swatches were weighed on an analytical balance and their starting weight was recorded. The hair swatches were immersed in either 5.0% ACB Pisum Sativum Peptide aqueous solution, 5.0% Wheat Hydrolysate aqueous solution (positive control) or left untreated (negative control). The treated swatches were immersed in their respective solutions for three hours at 22°C and then rinsed with deionized water. The hair swatches were air dried in the humidity controlled box (22°C, 50% Relative Humidity) for 48 hours. The swatches were then weighed and with the analytical balance for final measurement.

Oxygen Radical Absorbance Capacity (ORAC) Assay

info@activeconceptsllc.com • Phone: +1-704-276-7100 • Fax: +1-704-276-7101

Tradename: ACB Pisum Sativum Peptide

Code: 16810

CAS #: 90082-41-0

Test Request Form #: 33

Sponsor: *Active Concepts, LLC; 107 Technology Drive Lincolnton, NC 28092*
Study Director: *Erica Segura*
Principle Investigator: *Meghan Darley*

Test Performed:
Oxygen Radical Absorbance Capacity (ORAC) Assay

Introduction

Reactive oxygen species (ROS) are generated by normal cellular processes, environmental stresses, and UV irradiation. ROS are dangerous to cellular structures and functional molecules (i.e DNA, proteins, lipids) as they act as strong oxidizing agents or free radicals. The oxygen radical absorbance capacity (ORAC) assay is a standard method used to assess antioxidant capacity of physiological fluids, foods, beverages, and natural products. The assay quantitatively measures a sample's ability to quench free radicals that have the potential to react with and damage cellular components.

Oxygen Radical Absorbance Capacity (ORAC) assay was conducted to assess the antioxidant capacity of **ACB Pisum Sativum Peptide**.

Assay Principle

This assay is based upon the effect of peroxyl radicals generated from the thermal decomposition of 2, 2'-azobis-2-methyl-propanimidamide dihydrochloride (AAPH) on the signal intensity from the fluorescent probe, fluorescein, in the presence of an oxygen radical absorbing substance. The degree of change is indicative of the amount of radical damage and the presence of antioxidants results in an inhibition in the free radical damage to the fluorescein. The antioxidant protection of the sample can be calculated by comparing it to a set of known standards. Trolox®, a water soluble vitamin E analog, with known antioxidant capabilities is used in this ORAC assay as the standard for measuring the antioxidant capacity of unknown substances. ORAC values, expressed in µM of Trolox® equivalents (TE), are calculated using the area under the curves (AUC) of the test product, Trolox®, and the control materials. Trolox equivalency is used as the benchmark for antioxidant capacity of mixtures since it is difficult to measure individual components.

Reactive Oxygen Species Scavenging Assay

info@activeconceptsllc.com • Phone: +1-704-276-7100 • Fax: +1-704-276-7101

Tradename: ACB Pisum Sativum Peptide

Code: 16810

CAS #: 90082-41-0

Test Request Form #: 8392

Lot #: 8380400

Sponsor: *Active Concepts, LLC; 107 Technology Drive Lincolnton, NC 28092*
Study Director: *Maureen Danaher*
Principle Investigator: *Daniel Shill*

Test Performed:
Reactive Oxygen Species Scavenging Assay

Introduction

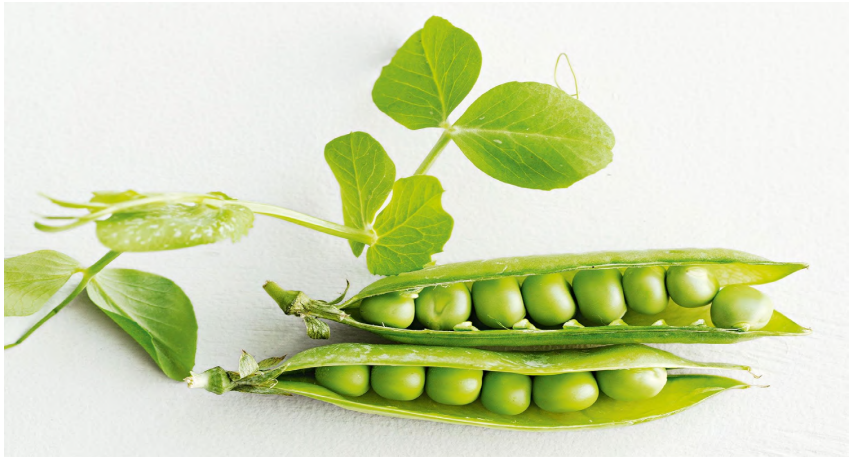
Low levels of intracellular oxidative stress are produced during normal physiological functions. However, UV irradiation, pollutants, foreign substances, and aging elicit unrestricted increases in reactive oxygen species (ROS). These deregulated augmentations in oxidative stress lead to an acceleration of DNA mutation, cellular senescence, advanced glycation end products, protein oxidation, and collagen degradation. Moreover, when intrinsic antioxidant capacities are reduced, such as during aging, an imbalance between pro- and anti-oxidant systems further accentuates these hallmarks of cellular aging.

Accordingly, a ROS Scavenging Assay was conducted to assess the *in vitro* effect of **ACB Pisum Sativum Peptide** to scavenge unnecessary oxidative stress in dermal fibroblasts. Attenuating excessive ROS preserves cellular homeostasis and blunts intrinsic and extrinsic age-related declines in skin cell function.

Assay Principle

Two cell-permeant dyes, CellROX™ Orange Reagent and Hoechst, were utilized in conjunction to provide a specific and quantitative method for determining ROS levels. CellROX™ Orange Reagent fluoresces brightly when bound to ROS indicating oxidative stress, and Hoechst fluoresces when bound to nuclear DNA to indicate cellular nuclei. By displaying the relative fluorescent units (RFU) from the CellROX™ Orange Reagent (ROS Signal) as a function of Hoechst (Nuclear Signal), ROS can be quantified and normalized at the cellular level. To elicit supraphysiological mitochondrial- and non-mitochondrial-derived levels of oxidative stress, the cells were exposed to Antimycin A, a complex III inhibitor of the mitochondrial electron transport chain.

Salon Half-Head Study



pisum sativum
key to anti-aging hair care
volumizing . Hydrating
film former + moisturizing
with efficacious
antioxidant protection

ABSTRACT

The condition of the cuticle (the outer most layer of the hair) significantly affects both the manageability and sleekness of our hair. Over time, hair can become damaged, which can result in the cuticle lifting because of both environmental and styling influences and processes. The result: lifeless, dull hair that is difficult to manage. Improving the sleekness of hair has been shown to instantly create a healthier more youthful appearance. Increasing combability not only eases manageability, but also helps to minimize physical damage that perpetuates the loss of body and difficulty in styling.

ACB Pisum Sativum Peptide is a product designed to increase the volume of the hair while providing hydration and antioxidant properties for protection against stressors. However this unique ingredient also enhances shine, dry and wet combability, manageability and the smoothness of the hair. The purpose of this study was to confirm whether or not **ACB Pisum Sativum Peptide** is capable of providing these additional benefits in a shampoo and conditioner application.

A half head study was conducted to determine the comparison of a control shampoo vs. 2.0% **ACB Pisum Sativum Peptide** in the control shampoo. Additionally, a comparison between the control conditioner and 2.0% **ACB Pisum Sativum Peptide** in the control conditioner were reported. Each volunteer's hair was photographed prior to the treatment and again after the shampoo and conditioner had been applied and the hair was styled. The images of the half head study were used in conjunction with a sensory assessment subjectively rating the parameters - cleansing, smoothing, dry and wet combability, anti-frizz, overall feel, shine and hydration. This assessment was conducted both before and after treatment. Based on the results obtained, **ACB Pisum Sativum Peptide** is capable of enhancing wet and dry combability, anti-frizz, overall feel, shine and hydration of the hair. These attributes make it an ideal ingredient for use in products intended for all hair types.

Code Number: 16810

INCI Name: Pisum Sativum (Pea) Peptide
INCI Status: Conforms
REACH Status: Complies
CAS Number: 90082-41-0
EINECS Number: 290-130-6

TRF#: S787
Lot Number(s): 65212P

Suggested Use Levels: 1.0 - 5.00%
Use Level for Assay: 2.00%

Sponsor:
Active Concepts, LLC
107 Technology Drive
Lincolnton, North Carolina 28092

Study Director: Maureen Danaher
Principle Investigator:
Candice Sneed

Suggested Applications:
Anti-aging, Hair and Skin Care, Antioxidant, Volumizing, Smoothing, Hydrating

Benefits of **ACB Pisum Sativum Peptide**:

- Anti-Aging Skin & Hair Care
- Maximizes Hair Volume
- Scalp and Follicle Health
- Increases Hydration
- Antioxidant Protection

Active Concepts

info@activeconceptsllc.com • Phone: +1-704-276-7100 • Fax: +1-704-276-7101

Sirius Red/Fast Green Collagen Analysis

Tradename: ACB Pisum Sativum Peptide

Code: 16810

Lot #: 33396

CAS #: 90082-41-0

Test Request Form #: 949

Sponsor: *Active Concepts, LLC; 107 Technology Drive Lincolnton, NC 28092*
Study Director: *Erica Segura*
Principle Investigator: *Meghan Darley*

Test Performed:
Sirius Red/Fast Green Collagen Assay

Introduction

Collagen is the main protein of connective tissues, such as skin, bone, tendon and ligament, and the most abundant protein in mammals. Collagen accounts for nearly 25% to 35% of the total human protein content. Collagen is a long, fibrous protein that forms bundles called fibers giving structure and support to cells and tissues. Collagen has great tensile strength and is responsible for skin's elasticity and, therefore, its degradation leads to wrinkles that accompany aging.

Sirius Red/Fast Green Collagen Assay was conducted to assess the changes in collagen synthesis by **ACB Pisum Sativum Peptide** treated *in vitro* cultured human dermal fibroblasts.

Assay Principle

Sirius Red is a unique dye that binds specifically to the helical structure of types I through V collagen, while Fast Green binds to non-collagenous proteins. These two dyes work in conjunction to provide a semi-quantitative method of determining amounts of collagen and non-collagenous proteins in a sample. After staining a sample the dyes are easily extracted and have optical density (OD) absorptions at 540nm (Sirius Red) and 605nm (Fast Green). Protein concentrations are calculated through equations with OD values.

@activeconceptsllc.com • Phone: +1-704-276-7100 • Fax: +1-704-276-7101

TGF-β1 ELISA Analysis

Tradename: ACB Pisum Sativum Peptide

Code: 16810

CAS #: 90082-41-0

Test Request Form #: 1460

Lot #: 40996

Sponsor: *Active Concepts, LLC; 107 Technology Drive Lincolnton, NC 28092*
Study Director: *Erica Segura*
Principle Investigator: *Meghan Darley*

Test Performed:
Transforming Growth Factor 1 (TGF- 1) Enzyme-Linked Immunosorbent Assay (ELISA)

Introduction

Transforming Growth Factor beta (TGF-) is a pleiotropic cytokine which exists in five isoforms, known as TGF- 1-5, with homologies of 70-80%[1]. TGF- 1 is the most abundant isoform and is highly conserved, with 100% sequence homology between the human, simian, bovine, porcine, and chicken proteins and 99% homology between the human and murine proteins[1]. TGF- plays a critical role cell cycle regulation and apoptosis. Male pattern baldness is an apoptosis-driven process resulting in early entry into the catagen hair cycle phase[2]. It has also been shown that TGF- 1 expression is highest in the late anagen phase and early catagen phase suggesting an important role in hair cycle regulation[3]. Inhibition of TGF- is believed to slow regression into the catagen hair cycle phase and result in follicle and hair shaft retention and prevention of hair loss[4].

Transforming Growth Factor- ELISA was conducted to assess the changes in TGF- levels in **ACB Pisum Sativum Peptide**-treated *in vitro* cultured Normal Human Dermal Fibroblasts.

1. Human/Mouse TGF beta 1 ELISA Ready-SET-Go! (Second Genetration). *eBioscience*® (2009)
2. Yumika Tsuji, *et. al.*. A Potential Suppressor of TGF- Delays Catagen Progression in Hair Follicles. *JID Symposium Proceedings*, 8: 65-68 (2003)
3. Kerstin Foitzik, *et. al.* Control of the murine hair follicle regression (catagen) by TGF- 1 *in vivo*. *FASEB J*, 14: 752-760 (2000)
4. Roberta Mazzieri, *et al.* Expression of a truncated latent TGF- -binding protein modulates TGF- signaling. *J. Cell Sci.118: 2177-2187 (2005)*

Active Concepts

info@activeconceptsllc.com • Phone: +1-704-276-7100 • Fax: +1-704-276-7101

Volumizing Assay

Tradename: ACB Pisum Sativum Peptide

Code: 16810

Lot #: NC180315-F

CAS #: 100209-45-8

Test Request Form #: 4643

Sponsor: *Active Concepts, LLC; 107 Technology Drive Lincolnton, NC 28092*
Study Director: *Erica Segura*
Principle Investigator: *Maureen Danaher*

Test Performed:
Volumizing Assay

Abstract

Hydrolyzed proteins, such as Oat, Soy and Wheat have been used in hair care as a traditional means to hydrate the hair and provide strengthening properties. Until recently, hydrolysis was induced using acid, water, or fermentation. Active Concepts has implemented an innovative hydrolysis approach to the newest and most bio-available vegetable protein on the market, Pisum Sativum Peptide. This microorganism prompted hydrolysis creates the by product, lactic acid, as a secretion which provides volumizing and anti-aging benefits measured.

Materials and Methods

The hair samples used in this study were tested using identical intervals and percentages of two protein hydrolysates, **ACB Pisum Sativum Peptide** and Wheat Hydrolysate. The materials used in the procedure to determine the diameter of each strand were an untreated control hair sample, the control hair sample (treated with 2.0% Wheat Hydrolysate Solution), and the sample treated with the test material (2.0% **ACB Pisum Sativum Peptide**). Each hair was imaged and measured before a solution was applied. The hairs were then removed from the slide and either placed in the 2.0% solution of the Wheat Hydrolysate or the 2.0% solution of **ACB Pisum Sativum Peptide**. Each hair was removed, measured and imaged then placed aside. After four hours, each hair was reimaged and measured to demonstrate sustained volume potential of each respective hydrolyzed protein.

Int J Trichology. 2012 Jul-Sep; 4(3): 185–186. doi: 10.4103/0974-7753.100096

PMCID: PMC3500065 PMID: 23180935

Role of Caffeine in the Management of Androgenetic Alopecia

Manish Bansal, Kajal Manchanda, and Shyam Sunder Pandey

Androgenetic alopecia (AGA) is hereditary and androgen-dependent, progressive thinning of the scalp hair that follows a defined pattern. It is a common dermatological problem affecting both men and women, with significant negative impact on their social and psychological well being.[1] It commonly begins by 20 years of age and affects nearly 50% of men by the age of 50 years.[1] Its etiopathogenesis is mainly androgen dependent and modulated via the testosterone metabolite dihydrotestosterone (DHT) and the expression of hair follicle-related androgen receptor.[2] The genetic factors also have been implicated in the pathogenesis of AGA.[2] Patients afflicted with AGA suffer from severe impairment of quality of life and thus treatment of this condition is mandatory, requiring long-term treatment with chief concerns about the efficacy and safety of the product used. Currently only oral finasteride and topical minoxidil are approved for treatment of AGA.[3,4] Recently, certain newer advances have shown caffeine to have beneficial effects in patients suffering from AGA. The proposed mechanism which would counteract DHT-induced miniaturization of the hair follicle include inhibition of phosphodiesterase by caffeine, which increases cAMP levels in cells and therefore promotes proliferation by stimulating cell metabolism.[5] A study conducted by Fischer et al. used hair organ culture model to investigate the effects of testosterone and caffeine on hair follicle growth stimulation. This in vitro study used scalp biopsy samples from male AGA patients which were cultivated using different concentrations of testosterone and/or caffeine for a period of 120-192 hours. Addition of caffeine in concentrations of 0.001% and 0.005% were found to counteract the suppressive effects of testosterone on hair growth, with a higher hair shaft elongation seen at 120 h after caffeine administration, compared to control group. This in vitro study thus clearly demonstrates that caffeine is a stimulator of human hair growth which may have importance in the treatment of AGA.[5] Brandner et al. proved by their double-blind placebo-controlled trial that caffeine application causes a substantial reduction in the transepidermal water loss in men compared to women, thus improving barrier function in men.[6] Regarding the route of delivery of caffeine, hair follicles are considered an important route for drug delivery. A recent study which assessed the follicular penetration of topical caffeine in hair follicles proved hair follicles to be faster route of drug delivery for topically applied drugs.[7] An important requirement for the treatment of AGA is follicular drug delivery. A recent study assessed the follicular penetration of caffeine on topical application in a shampoo formulation for 2 min and showed that penetration via hair follicles was faster and higher compared with the interfollicular route and that hair follicles were the only pathway for faster caffeine absorption during the first 20 min after application.[8]

The beneficial effects of topical application of caffeine in AGA can thus be attributed to inhibition of phosphodiesterase, improvement in barrier function, follicular penetration, stimulation and promotion of hair growth. Thus it appears to be a useful adjuvant in the management of AGA. However, further studies need to be done to confirm and establish the role of caffeine in management of AGA.

REFERENCES

1. Ellis JA, Sinclair R, Harrap SB. Androgenetic alopecia: pathogenesis and potential for therapy. Expert Rev Mol Med. 2002;2:1–11. [PubMed] [Google Scholar]

2. Trüeb RM. Molecular mechanisms of androgenetic alopecia. Exp Gerontol. 2002;37:981–90. [PubMed] [Google Scholar]

3. Kaufman KD, Olsen EA, Whiting D, Savin R, DeVillez R, Bergfeld W, et al. Finasteride in the treatment of men with androgenetic alopecia. Finasteride male pattern hair loss Study Group. J Am Acad Dermatol. 1998;39(4 Pt 1):578–89. [PubMed] [Google Scholar]

4. Price VH. Treatment of hair loss. N Engl J Med. 1999;341:964–73. [PubMed] [Google Scholar]

5. Fischer TW, Hipler UC, Elsner P. Effect of caffeine and testosterone on the proliferation of human hair follicles in vitro. Int J Dermatol. 2007;46:27–35. [PubMed] [Google Scholar]

6. Brandner JM, Behne MJ, Huesing B, Moll I. Caffeine improves barrier function in male skin. Int J Cosmet Sci. 2006;28:343–7. [PubMed] [Google Scholar]

7. Otberg N, Patzelt A, Rasulev U, Hagemeister T, Linscheid M, Sinkgraven R, et al. The role of hair follicles in the percutaneous absorption of caffeine. Br J Clin Pharmacol. 2007;65:488–92. [PMC free article] [PubMed] [Google Scholar]

8. Otberg N, Teichmann A, Rasuljev U, Sinkgraven R, Sterry W, Lademann J. Follicular penetration of topically applied caffeine via a shampoo formulation. Skin Pharmacol Physiol. 2007;20:195–8. [PubMed] [Google Scholar]

Skin Pharmacol Physiol. 2018 Jan; 30(6): 298–305. Published online 2017 Oct 21. doi: 10.1159/000481141 PMCID: PMC5804833 PMID: 29055953

An Open-Label Randomized Multicenter Study Assessing the Noninferiority of a Caffeine-Based Topical Liquid 0.2% versus Minoxidil 5% Solution in Male Androgenetic Alopecia

Rachita Dhurat,a Jill Chitallia,a Theodor W. May,f Ammani M. Jayaraaman,b Jithendriya Madhukara,d Subbu Anandan,c Pradyumna Vaidya,e and Adolf Klenkg,*

Abstract

Background

Androgenetic alopecia is a condition with a high prevalence worldwide and affects both males and females. Currently, only 2 approved treatments exist: finasteride (males only) and minoxidil 2 or 5% solution (males and females).

Methods

We conducted a randomized, open-label, multicenter noninferiority study to determine whether a caffeine-based 0.2% topical liquid would be no less effective than minoxidil 5% solution in males (n = 210) with androgenetic alopecia. The primary end point was the percentage change in the proportion of anagen hairs from baseline to 6 months using a frontal and occipital trichogram.

Results

At 6 months, the group of the 5% minoxidil solution showed a mean improvement in anagen ratio of the trichogram of 11.68%, and the group of the 0.2% caffeine solution had an anagen improvement of 10.59%. The difference of mean values between both groups was 1.09%. The statistical analysis was performed and reported in accordance with the CONSORT Guidelines 2010 for reporting of noninferiority and equivalence randomized trials.

Conclusion

A caffeine-based topical liquid should be considered as not inferior to minoxidil 5% solution in men with androgenetic alopecia.

Keywords: Androgenetic alopecia, Caffeine-based topical liquid, Anagen hairs, Frontal trichogram, Occipital trichogram

Introduction

Androgenetic alopecia (AGA) is the most common hair loss disorder worldwide, affecting up to 80% of Caucasian men aged older than 70 years. Although the prevalence of AGA is high in elderly subjects, the first signs often develop during puberty. Hair loss can have substantial impacts on quality of life, including negative effects on self-esteem and perceived physical attractiveness, and may even lead to depression. Despite these negative effects, many patients do not pursue preventative therapy for hair loss, and many of those that try therapies that promise hair regrowth are dissatisfied when they first go to see a specialist. Limited efficacy, poor tolerance, and lack of information on treatment duration or adverse events (AEs) may result in reduced compliance to a long-term therapeutic regimen [1].

The hair follicle has 3 main lifecycle stages. Anagen is the active growth phase of hair follicles in which the root of the hair is dividing rapidly and adding to the length of the hair shaft. Scalp hair normally stays in this active phase of growth for 2–6 years [2]. Following the anagen phase, the hair shaft enters into the catagen phase, and hair follicles undergo a highly controlled process of involution that largely reflects a burst of programmed cell death of the majority of follicular keratinocytes. The third and last stage is the telogen phase, during which the hair shaft matures into a club hair and is then shed from the follicle, usually during washing or combing.

Hair loss and unwanted hair growth both reflect aberrations in hair follicle cycling, and consequently, in principle, they may be reversed. AGA is caused by the progressive shortening of successive anagen phases as well as the gradual miniaturization of genetically predisposed follicles in the presence of androgens; in addition, large, pigmented hairs (terminal hairs) are replaced by thin lightly pigmented hair (vellus hair). Due to the presence of these cycling hair follicles, AGA is considered to be potentially reversible. However, simply removing androgens does not often result in the conversion of miniaturized follicles to terminal follicles. Therefore treatments utilizing other lines of approach are needed [3].

Currently, there are few approved treatments on the market for AGA. The only FDA-approved treatments for AGA are finasteride, taken orally (males only), and topical minoxidil 2 or 5% solution (females and males) [4, 5, 6, 7].

Minoxidil (Rogaine; H + H Pharmaceuticals) is an androgen-independent medication that counteracts AGA by causing premature termination of the telogen phase and likely prolongs the anagen phase [8]. There appear to be differences in efficacy between the 2 and 5% concentrations. In a study of 393 men with AGA, a 5% minoxidil solution demonstrated significantly greater efficacy, compared with the 2% minoxidil solution [8].

In recent years, caffeine has demonstrated potential as a treatment for AGA [9]. Due to being a phosphodiesterase inhibitor, caffeine increases cyclic adenosine monophosphate levels in cells and consequently promotes cell proliferation through stimulating cell metabolism - a mechanism that may counteract testosterone/dihydrotestosterone-induced miniaturization of the hair follicle [10]. In a male skin organ culture model, caffeine reversed the inhibiting effect of testosterone on keratinocyte proliferation [11]. In an in vitro study, testosterone-induced hair follicle growth suppression was reversed with addition of caffeine at concentrations of 0.001 and 0.005%; moreover, caffeine alone led to significant stimulation of hair follicle growth [10]. In another in vitro study of male and female hair follicles, caffeine was found to enhance hair shaft elongation, prolong anagen duration and stimulate hair matrix keratinocyte proliferation. In addition, hair follicles from females appeared to be more sensitive to caffeine than hair follicles from males, and caffeine counteracted testosterone-induced transforming growth factor-β2 expression, a major antagonistic hair growth regulatory factor, in male hair follicles. Caffeine also resulted in increased expression of insulin-like growth factor-1, a promoter of hair growth, in both male and female hair follicles [12]. Notwithstanding that these findings are results of in vitro experiments, the topical treatment of caffeine in vivo is also promising because of its good absorption and follicular penetration [13].

Caffeine has also been shown to penetrate the hair follicle even when applied as a shampoo formulation. In a study of 6 male volunteers, a caffeine-based shampoo (Alpecin; Dr. Kurt Wolff GmbH) resulted in penetration of caffeine into both the stratum corneum and hair follicles after 2-min application, with the highest values being found 2 h after application [14].

The potential efficacy of a caffeine-based topical formulation has been previously demonstrated in a prospective study of 40 men with AGA. In this study, daily use of the caffeine-based lotion resulted in an 8.14% reduction in hairs extracted at 2 months and a 15.33% reduction in hairs extracted at 4 months. In addition, at 2 and 4 months, 75 and 83% of participants were considered to have had a positive response (decrease in number of pull test hairs) [15]. However, this study only had one arm and, consequently, was noncomparative, and therefore one cannot draw too many conclusions from the results.

Here, results are reported from a noninferiority study that aimed to determine whether a caffeine-based topical 0.2% liquid is no less effective than minoxidil 5% solution in males with AGA.

The design of a noninferiority study, to demonstrate the efficacy of the caffeine solution, seemed more appropriate than a placebo-controlled study design, because the reference product is the FDA-approved ingredient minoxidil. Hence the effect of the test product can be directly compared with an approved reference.

Methods

Study Design

This was a registered, prospective, open-label, randomized, active-controlled study conducted at 5 centers in India (CTRI/ 2014/07/004768, registered on July 25, 2014): Lokmanya Tilak Municipal General Hospital, Mumbai; St. John Medical College and Hospital, Bengaluru; Sri Ramachandra Medical College and Hospital, Chennai; Jehangir Clinical Development Center, Pune; Chennai Meenakshi Multi Specialty Hospital, Chennai. Ethical votes have been approved for all study sites. The study period included 4 visits to the study center: visit 1 (screening, conducted 3 days prior to baseline visit), visit 2 (baseline, day 1), visit 3 (treatment visit; day 90/month 3), and visit 4 (end-of-study visit; day 180/month 6). There was a 3-day hair wash quarantine before visits 3 and 4.

Subjects were randomized in a 1:1 ratio to either a caffeine-based topical liquid (treatment group A; test product) or minoxidil 5% solution (treatment group B; reference product).

Subjects

This study included males aged between 18 and 55 years with AGA. Additional inclusion criteria were: balding stage of III-V on the Hamilton-Norwood scale [16] and use of global photography to confirm the Hamilton-Norwood stage of balding, at least 20% telogen ratio in the trichogram, and a willingness to participate and provide signed informed consent. Exclusion criteria were: diagnosis of pathological forms of alopecia (such as alopecia areata, trichotillomania, scarring alopecia, and alopecia due to medication), diagnosis of dermatological conditions (such as eczema, fungal scalp conditions, seborrheic dermatitis, recurrent herpes, pityriasis versicolor, psoriasis, pigmentary disorders, chronic lupus erythematosus), history of chemotherapy, and known hypersensitivity to minoxidil 5% solution or Alpecin that could interfere directly/indirectly with the study.

Interventions

The test product, 0.2% caffeine solution, is marketed as Alpecin Liquid by Dr. Kurt Wolff and distributed by the study sponsor Fullife Healthcare Pvt Ltd. The control product is a 5% minoxidil solution, marketed as Mx-5 by H + H Pharmaceuticals PvT Ltd. Subjects in the 0.2% caffeine solution arm were instructed to apply 2 mL of the test product to the scalp twice a day (once in the morning and once in the evening), and subjects in the minoxidil 5% solution arm were instructed to apply 1

mL of the reference product to the scalp twice a day (once in the morning and once in the evening). The active treatment period duration was 6 months.

Primary Outcome

The primary end point was the percentage change in proportion of anagen hairs, or the anagen rate (AR), from baseline to 6 months using frontal and occipital trichograms in the per-protocol (PP) population.

In this study, hair loss was assessed with trichograms in the frontal and occipital areas of the scalp. A trichogram involves the microscopic examination of hairs plucked from the scalp and provides information about both the hair root and the hair tip. A set number of hairs are removed and examined per trichogram. The hairs are arranged side by side on a glass slide and taped, and are then examined under a microscope. Examination of the proximal end of the hair shaft (the hair root) can help determine whether the hair is in anagen, telogen, or catagen phase and whether it is normal or dystrophic [17].

Secondary Outcomes

Secondary end points were the separate percentage changes in AR from baseline to 3 and 6 months using frontal and occipital trichograms, changes in number of subjects with an increase in anagen hair (and decrease in telogen hair) using a frontal trichogram from baseline to 3 and 6 months, changes in number of subjects with increase in anagen hair (and decrease in telogen hair) using an occipital trichogram from baseline to 3 and 6 months, change in subject's perception of effect of the caffeine-based topical 0.2% liquid or minoxidil 5% solution on hair loss management, assessed with a subject questionnaire from baseline to 3 and 6 months, and change in clinical effect as assessed by a dermatologist questionnaire from baseline to 3 and 6 months.

Safety was also assessed: incidence of AEs during the study period and changes in vital signs from baseline to 6 months.

Sample Size Calculation

The calculation of the sample size was based on the noninferiority margin for the difference in ARs of 5% using a 2-sided t test (assuming a common standard deviation of AR by 10%). A sample size of 176 subjects was calculated to be sufficient to reject the hypothesis of inferiority with a 90% power and an alpha error level of 0.05%. In total, 210 subjects were required, assuming a dropout rate of approximately 15%.

Randomization and Blinding

The randomization list (balanced randomization with a block size of 6) was generated by Dr. Kurt Wolff GmbH & Co. KG using a validated computer program (RANCODE, IDV Gauting) and sent to Fullife Healthcare Pvt Ltd., who then provided envelopes to the study sites containing the subject randomization details.

A blinding of probands and examiners was not intended, because the dosing in both arms was different. In the control arm of 5% minoxidil the regular dose was 1 mL twice per day, in the 0.2% caffeine solution arm the dosing was 2 mL twice per day.

Statistical Analysis

The statistical analysis was performed and reported in accordance with the CONSORT Guidelines 2010 for reporting of noninferiority and equivalence randomized trials [18]. The primary aim of this

study was to demonstrate noninferiority of a caffeine-based topical 0.2% liquid to minoxidil 5% solution in subjects with AGA. The primary outcome measure was analyzed primarily for the PP population and repeated for sensitivity reasons for the intention-to-treat (ITT) population. The 2-sided 95% confidence interval approach was used to test noninferiority [18, FDA Guidelines 2016]. In addition, analyses of covariance (ANCOVAs) were performed to evaluate the difference between treatment arms in ARs after 6 months (using AR at baseline as a covariate).

Analyses of secondary efficacy end points were based on nonparametric tests (2-sided Mann-Whitney test and the Friedman test), due to the nonnormal distribution of the data, as well as the Fisher exact text (for categorical data) at the 5% level of significance ($p < 0.05$).

All randomized probands were included in these analyses, and missing values were not replaced. Statistical tests were performed as 2-sided tests with an alpha error of 0.05. However, statistical testing of all secondary end points was explorative and not confirmatory.

Results

Overall, 210 subjects were enrolled and randomized to treatment arms; the PP population comprised 161 subjects. For a CONSORT flow diagram, see Figure Figure11.

An external file that holds a picture, illustration, etc.

Object name is spp-0030-0298-g01.jpg

Fig. 1

CONSORT flow diagram. PPS, per protocol set.

Patient Characteristics

The median age of the subjects was 31.0 (range 19–50) and 29.0 (range 21–51) years in the caffeine-based topical 0.2% liquid and minoxidil 5% solution arms, respectively; the mean age was 32.2 (standard deviation 7.3) and 31.1 (7.6) years, respectively. There were no significant differences in baseline characteristics between treatment arms (Table (Table1);1); however, the number of anagen, telogen, and dystrophic hairs extracted from subjects at baseline significantly differed ($p < 0.01$) in 1 study center from the other 4 centers. Reasons for that could be differences in the study population. In 1 center the percentage of young and working people was higher. These people could have experienced psychological stress or nutritional deficiencies in addition to their predisposition of AGA which could explain the higher percentage of telogen hairs. The higher telogen rate in the differing center did not change the outcome of the noninferiority between both study arms.

Table 1

Characteristics of study subjects at baseline

	Caffeine-based topical 0.2% liquid (n = 105)	Minoxidil 5% solution (n = 105)
Hamilton-Norwood stage, % subjects		
Grade III	28.6	28.6
Grade III vertex	17.1	22.9

Grade IIIA	7.6	15.2
Grade IV	28.6	20.0
Grade IVA	3.8	2.9
Grade V	14.3	10.5
Telogen hairs, mean %	36.5	36.2
Frontal trichogram		
Anagen hairs	36.4 (13.7)/39 (0–60)	35.3 (15.7)/41 (0–62)
Telogen hairs	29.2 (9.5)/28 (13–69)	28.7 (9.6)/27 (10–75)
Dystrophic hairs	8.2 (7.6)/6 (0–29)	9.6 (9.6)/7 (0–42)
Total hair count	73.8 (8.2)/73 (60–100)	73.6 (8.0)/73 (60–97)
Occipital trichogram		
Anagen hairs	40.7 (16.4)/46 (1–74)	39.4 (18.3)/44 (0–74)
Telogen hairs	25.0 (10.5)/23 (8–76)	24.8 (10.3)/24 (6–65)
Dystrophic hairs	9.6 (10.1)/7 (0–44)	10.7 (11.4)/8 (0–50)
Total hair count	75.4 (8.0)/74 (61–95)	74.9 (8.0)/74 (61–95)
Frontal + occipital trichogram		
Anagen hairs	77.2 (28.8)/85 (1–134)	74.7 (33.3)/87 (1–135)
Telogen hairs	54.2 (17.3)/51 (26–145)	53.5 (18.0)/51 (27–140)
Dystrophic hairs	17.8 (16.4)/16 (0–64)	20.4 (20.3)/16 (0–80)
Total hair count	149.1 (13.4)/147 (123–180)	148.6 (13.1)/148 (123–177)

Open in a separate window

For trichogram data, mean numbers with standard deviations in parentheses are given, followed by medians with ranges in parentheses.

Efficacy Outcomes

Primary Efficacy Analysis At 6 months, minoxidil 5% solution was associated with a nonsignificantly higher increase from baseline in AR, compared with the caffeine-based topical 0.2% liquid (11.68 ± 12.44 vs. 10.59 ± 12.02% in the PP population; p = 0.574), using frontal and occipital trichograms (Table (Table2).2). The 2-sided 95% CI for the difference in the mean increase in AR between treatment arms (1.09%) ranged from −2.72 to 4.89%. The upper limit of the 95% CI below the predetermined margin for noninferiority of 5% was not exceeded, and consequently the caffeine-based topical 0.2% liquid was determined to be noninferior to the minoxidil 5% solution (Fig. (Fig.22).

An external file that holds a picture, illustration, etc.

Object name is spp-0030-0298-g02.jpg

Fig. 2

Mean (±standard error, SE) of the rate of anagen hair (AR; %) by treatment and visit (baseline, after 3 months, and after 6 months).

Table 2

Change in percentage of anagen hairs from baseline to 3 and 6 months in the per-protocol population using frontal and occipital trichograms

	Caffeine-based topical 0.2% liquid (n = 82)	Minoxidil 5% solution (n = 79)
Baseline	53.01 (17.13)/59.37 (0.7–76.6)	50.81 (19.33)/56.86 (0.8–77.3)
3 months	58.76 (19.75)/67.42 (3.8–83.1)	57.15 (20.94)/65.45 (2.4–80.0)
6 months	63.60 (21.43)/74.75 (5.7–82.1)	62.49 (22.47)/72.86 (4.8–83.2)

Open in a separate window

Results are expressed as means with standard deviations in parentheses, followed by medians with ranges in parentheses.

A similar outcome was observed in the ITT population. At 6 months, increases in AR were not significantly different between the caffeine-based topical 0.2% liquid and minoxidil 5% solution arms (10.18 ± 11.83 vs. 11.34 ± 12.03%; p = 0.504). The 2-sided 95% CI for the difference in mean increase in AR (1.16%) ranged from −2.25 to 4.56%. The upper limit of the 95% CI was lower than the prespecified noninferiority margin of 5%.

ANCOVAs of the AR (in percent) after 6 months (using baseline values as covariate) confirmed that there was no significant treatment effect (difference between groups) in both population sets (PP and ITT).

In addition, ANCOVAs were performed including “center” as factor. In both population sets (PP and ITT), the effect of “center” was highly significant. However, neither in the PP nor in the ITT population was the margin of noninferiority violated.

Secondary Efficacy Analysis

Using only the frontal trichogram, there was no significant difference in the increase from baseline in AR at 6 months between the caffeine-based topical 0.2% liquid and minoxidil 5% solution arms (11.27 ± 13.02 vs. 11.89 ± 11.78%; p = 0.740). The corresponding 2-sided 95% CI for the difference in mean increases in AR (0.62%) ranged from −3.06 to 4.30%.

Using only the occipital trichogram, there was no significant difference in the increase from baseline in AR at 6 months between the caffeine-based topical 0.2% liquid and minoxidil 5% solution arms (9.15 ± 13.14 vs. 11.08 ± 14.33%; p = 0.349). The corresponding 2-sided 95% CI for the difference in mean increases in AR (1.94%) ranged from −2.13 to 6.00%.

In addition, there were no significant differences at 6 months in the number of subjects for whom anagen hair increased and telogen hair decreased from baseline, using both the frontal trichogram ($p = 1.000$) and the occipital trichogram ($p = 0.310$) assessments.

With respect to subject assessments, subjects in both treatment arms considered the intensity of hair loss, the number of hairs falling out while combing, and hair thickness to be significantly improved from baseline at 6 months (all $p < 0.01$), with no significant differences between treatment arms at 6 months. At 3 months, subjects using minoxidil 5% solution reported significantly higher treatment satisfaction, compared with subjects using the caffeine-based topical 0.2% liquid ($p = 0.020$); however, by 6 months this difference was no longer significant ($p = 0.090$). Subjects using the caffeine-based topical 0.2% liquid reported significant improvement from baseline in scalp itchiness at 6 months ($p = 0.003$) whereas subjects using minoxidil 5% solution reported no such improvement ($p = 0.211$). However, the difference between arms was not significant at 6 months. Subjects in both groups reported a significant improvement in scalp tension/dryness ($p < 0.05$), with no significant difference between groups at 6 months.

With respect to investigator assessments, hair strength, balding progression, and extent of hair loss were considered to be significantly improved from baseline in both treatment arms at 6 months (all $p < 0.01$), with no significant differences between treatment arms. At 6 months, investigators recommended the study product in 97.8% of subjects using the caffeine-based topical 0.2% liquid and in 100% of subjects using minoxidil 5% solution. Investigators considered scalp redness and scaling/dandruff to be significantly improved from baseline in both treatment arms at 6 months (all $p < 0.05$), with no significant differences between treatment arms.

Safety

One patient (1%) in the minoxidil 5% solution arm reported an AE (mild headache). This AE was not considered to be related to treatment.

Discussion

This study provides the first comparative in vivo proof of the noninferiority of caffeine against 5% minoxidil solution for AGA in males. In this study, a caffeine-based topical 0.2% liquid was found to be no less effective than minoxidil 5% solution regarding the percentage change from baseline in AR at 6 months in both the PP population (primary end point) and ITT population, using frontal and occipital trichograms. In addition, similar outcomes between treatment arms were observed regarding the increase from baseline in AR at 6 months using either the frontal trichogram or the occipital trichogram alone and the change from baseline in the number of subjects with an increase in anagen hair (and decrease in telogen hair) using a frontal or occipital trichogram at 3 and 6 months.

In this study, both the caffeine-based topical 0.2% liquid and minoxidil 5% solution appeared to be well tolerated. However, AEs associated with topical minoxidil at the lower FDA-approved concentration of 2% have been previously reported, including irritant and allergic contact dermatitis as well as allergic reactions to the nonactive ingredient propylene glycol - a compound found in some topical solutions, particularly if they are galenic in nature [19]. In our study, the 0.2% caffeine solution resulted in a significant improvement from baseline in scalp itchiness at 6 months whereas no such improvement was observed for minoxidil 5% solution.

The subject information of the control product among other AEs associated with topical solutions at both the 2 and 5% concentrations includes headache, feeling faint or dizzy, chest pains, rapid

heartbeat, increased weight, and fluid retention [20]. However, these AEs were not reported by subjects in our study.

A limitation of our study included its open-label design, which may have resulted in unintentional bias on the part of both investigators and subjects. With respect to generalizability of the study findings, the relatively broad inclusion criteria suggest external validity in the general population of men with AGA.

In conclusion, the results of this study are promising because they show that an effective natural ingredient like caffeine can be considered as an effective alternative treatment to common drug therapies against hair loss. As well as the fact that genetically predisposed hair loss can hardly be classified as a hair disease, its treatment with drugs might be of concern when taking risk/benefit profiles into account. Such ethical considerations become even more important when the treatment is applied or administered daily for the rest of the subject's life and has to be done lifelong and not just only within a shorter therapy period. Well-tolerated ingredients are prerequisites for safe treatment against hereditary alopecia, and the caffeine solution assessed in this study seemed to meet this requirement.

Statement of Ethics

From all study participants, a signed informed consent was obtained.

Disclosure Statement

Adolf Klenk is an employee of the sponsor Dr. Kurt Wolff GmbH & Co. KG. Theodor May is a consultant of Dr. Kurt Wolff GmbH & Co KG.

Go to:

References

1. Blumeyer A, Tosti A, Messenger A, Reygagne P, Del Marmol V, Spuls PI, et al. Evidence-based (S3) guideline for the treatment of androgenetic alopecia in women and in men. J Dtsch Dermatol Ges. 2011;9((suppl 6)):S1–S57. [PubMed] [Google Scholar]

2. Stenn K, Parimoo S, Zheng Y, Barrows T, Boucher M, Washenik K. Bioengineering the hair follicle. Organogenesis. 2007;3:6–13. [PMC free article] [PubMed] [Google Scholar]

3. Paus R, Cotsarelis G. The biology of hair follicles. N Engl J Med. 1999;341:491–497. [PubMed] [Google Scholar]

4. Torres F. Androgenetic, diffuse and senescent alopecia in men: practical evaluation and management. Curr Probl Dermatol. 2015;47:33–44. [PubMed] [Google Scholar]

5. US Food and Drug Administration Drug facts - minoxidil 2% solution. https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm078877.pdf (accessed March 1, 2017).

6. US Food and Drug Administration Approval letter - minoxidil 5% solution 2001. http://www.accessdata.fda.gov/drugsatfda_docs/anda/2001/075598Orig1s000.pdf (accessed March 1, 2017).

7. Pierard GE, Pierard-Franchimont C, Marks R, Elsner P. EEMCO guidance for the assessment of hair shedding and alopecia. Skin Pharmacol Physiol. 2004;17:98–110. [PubMed] [Google Scholar]

8. Olsen EA, Dunlap FE, Funicella T, Koperski JA, Swinehart JM, Tschen EH, et al. A randomized clinical trial of 5% topical minoxidil versus 2% topical minoxidil and placebo in the treatment of androgenetic alopecia in men. J Am Acad Dermatol. 2002;47:377–385. [PubMed] [Google Scholar]

9. Herman A, Herman AP. Caffeine's mechanisms of action and its cosmetic use. Skin Pharmacol Physiol. 2013;26:8–14. [PubMed] [Google Scholar]

10. Fischer TW, Hipler UC, Elsner P. Effect of caffeine and testosterone on the proliferation of human hair follicles in vitro. Int J Dermatol. 2007;46:27–35. [PubMed] [Google Scholar]

11. Tsianakas A, Hüsing B, Moll I. An ex vivo model of male skin - caffeine counteracts testosterone effects. Arch Dermatol Res. 2005;296:450. [Google Scholar]

12. Fischer TW, Herczeg-Lisztes E, Funk W, Zillikens D, Biro T, Paus R. Differential effects of caffeine on hair shaft elongation, matrix and outer root sheath keratinocyte proliferation, and transforming growth factor-beta2/insulin-like growth factor-1-mediated regulation of the hair cycle in male and female human hair follicles in vitro. Br J Dermatol. 2014;171:1031–1043. [PubMed] [Google Scholar]

13. Trauer S, Lademann J, Knorr F, Richter H, Liebsch M, Rozycki C, et al. Development of an in vitro modified skin absorption test for the investigation of the follicular penetration pathway of caffeine. Skin Pharmacol Physiol. 2010;23:320–327. [PubMed] [Google Scholar]

14. Otberg N, Teichmann A, Rasuljev U, Sinkgraven R, Sterry W, Lademann J. Follicular penetration of topically applied caffeine via a shampoo formulation. Skin Pharmacol Physiol. 2007;20:195–198. [PubMed] [Google Scholar]

15. Bussoletti C, Mastropietro F, Tolaini MV, Celleno L. Use of a cosmetic caffeine lotion in the treatment of male androgenetic alopecia. J Appl Cosmetol. 2011;29:167–180. [Google Scholar]

16. Norwood OT. Male pattern baldness: classification and incidence. South Med J. 1975;68:1359–1365. [PubMed] [Google Scholar]

17. Serrano-Falcon C, Fernandez-Pugnaire MA, Serrano-Ortega S. Hair and scalp evaluation: the trichogram. Actas Dermosifiliogr. 2013;104:867–876. [PubMed] [Google Scholar]

18. Piaggio G, Elbourne DR, Pocock SJ, Evans SJW, Altman DG, CONSORT Group Reporting of noninferiority and equivalence randomized trials. Extension of the CONSORT 2010 statement. JAMA. 2012;308:2594–2604. [PubMed] [Google Scholar]

19. Rossi A, Cantisani C, Melis L, Iorio A, Scali E, Calvieri S. Minoxidil use in dermatology, side effects and recent patents. Recent Pat Inflamm Allergy Drug Discov. 2012;6:130–136. [PubMed] [Google Scholar]

20. DrugsUpdate: Minoxidil information from DrugsUpdate. DrugsUpdatecom. http://www.drugsupdate.com/generic/view/318/Minoxidil (accessed April 21, 2017).

Phytother Res . 2013 Feb;27(2):212-7. doi: 10.1002/ptr.4712. Epub 2012 Apr 20.

Promotion of hair growth by Rosmarinus officinalis leaf extract

Kazuya Murata 1, Kazuma Noguchi, Masato Kondo, Mariko Onishi, Naoko Watanabe, Katsumasa Okamura, Hideaki Matsuda

Affiliations expand

PMID: 22517595 DOI: 10.1002/ptr.4712

Abstract

Topical administration of Rosmarinus officinalis leaf extract (RO-ext, 2 mg/day/mouse) improved hair regrowth in C57BL/6NCrSlc mice that experienced hair regrowth interruption induced by testosterone treatment. In addition, RO-ext promoted hair growth in C3H/He mice that had their dorsal areas shaved. To investigate the antiandrogenic activity mechanism of RO-ext, we focused on inhibition of testosterone 5α-reductase, which is well recognized as one of the most effective strategies for the treatment of androgenic alopecia. RO-ext showed inhibitory activity of 82.4% and 94.6% at 200 and 500 μg/mL, respectively. As an active constituent of 5α-reductase inhibition, 12-methoxycarnosic acid was identified with activity-guided fractionation. In addition, the extract of R. officinalis and 12-methoxycarnosic acid inhibited androgen-dependent proliferation of LNCaP cells as 64.5% and 66.7% at 5 μg/mL and 5 μM, respectively. These results suggest that they inhibit the binding of dihydrotestosterone to androgen receptors. Consequently, RO-ext is a promising crude drug for hair growth.

Randomized Controlled Trial Skinmed

. 2015 Jan-Feb;13(1):15-21.

Rosemary oil vs minoxidil 2% for the treatment of androgenetic alopecia: a randomized comparative trial

Yunes Panahi, Mohsen Taghizadeh, Eisa Tahmasbpour Marzony, Amirhossein Sahebkar

PMID: 25842469

Abstract

Rosmarinus officinalis L. is a medicinal plant with diverse activities including enhancement microcapillary perfusion. The present study aimed to investigate the clinical efficacy of rosemary oil in the treatment of androgenetic alopecia (AGA) and compare its effects with minoxidil 2%. Patients with AGA were randomly assigned to rosemary oil (n = 50) or minoxidil 2% (n = 50) for a period of 6 months. After a baseline visit, patients returned to the clinic for efficacy and safety evaluations every 3 months. A standardized professional microphotographic assessment of each volunteer was taken at the initial interview and after 3 and 6 months of the trial. No significant change was observed in the mean hair count at the 3-month endpoint, neither in the rosemary nor in the minoxidil group ($P > .05$). In contrast, both groups experienced a significant increase in hair count at the 6-month endpoint compared with the baseline and 3-month endpoint ($P < .05$). No significant difference was found between the study groups regarding hair count either at month 3 or month 6 (> .05). The frequencies of dry hair, greasy hair, and dandruff were not found to be significantly different from baseline at either month 3 or month 6 trial in the groups ($P > .05$). The frequency of scalp itching at the 3- and 6-month trial points was significantly higher compared with baseline in both groups ($P < .05$). Scalp itching, however, was more frequent in the minoxidil group at both assessed endpoints ($P < .05$). The findings of the present trial provided evidence with respect to the efficacy of rosemary oil in the treatment of AGA.