Capixyl™

Introduction on hair loss

The importance of hair in our lives cannot be overstated...

Whether men or women lose their hair, they lose much more than their natural, youthful appearance. People also lose their self-esteem and self-confidence…

Hair loss (alopecia) is a common problem affecting both men and women.

The most common one is androgenetic alopecia (AGA) which represent **95% of all hair loss**

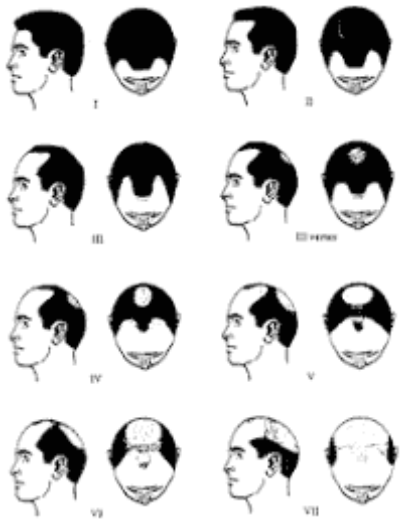
- Affects roughly 50% of men and perhaps as many women older than 40 years. By the age of 35, 2/3 of American men will experience some degree of appreciable hair loss. Approximately 25% of men who suffer with male pattern baldness begin the painful process before they reach the age of 21.
- Androgenetic alopecia affects an estimated 35M men in the USA and about 21M women.
- In France 10M of people are affected by hair loss, which represents 2 men out of 3 and 1 woman out of 5.
- In Japan, 30% of the male population experiences balding, usually after 45 years of age.
- The prevalence of AGA in Chinese men is 21.3% and 6% for women.

The causes of hair loss

Although causes of hair loss are still not yet fully understood, it can be the results of several factors.

Causes: Genetic;
Hormonal changes or imbalances (childbirth, menopause);
Improper nutrition (deficiency in certain vitamins and minerals);
Stress;
Diseases like diabetes or lupus;
Medications (drugs or chemotherapy);
Seasonal changes;
Aging & Photo-aging.

Hair loss can be **permanent** or **temporary**



Affects both men and women although men experience a much greater degree of loss (notably around the temples and the vertex) than women, but following menopause it may affect 75% of women older than 65 years.

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Market Opportunity?

According to The Washington Post, American hair loss sufferers spend more than **$3.5B** a year in an attempt to treat their hair loss.

There are numerous products on the market addressing this condition based on different mechanism of action:

•Vasodilation

The most popular are Minoxidil (Regain®/Rogain®) an OTC vasodilator medication known for its ability to slow or stop hair loss and promote hair regrowth (was discovered as adverse event)

****Minoxidil works on 1 person out of 2 & on younger people (18 to 40)*

Side effects: burning/irritation, redness the treated area, chest pain

•Hormonal (DHT transformation)

Finasteride (Propecia®) a drug that acts by inhibiting the enzyme that converts testosterone to dihydrotestosterone (DHT) in androgenic alopecia

Propecia® (finasteride) 1 mg
Helping make hair loss history®

• Collagen rigidification & hair anchoring

Aminexil® a patented molecule by L'Oréal fights against the stiffening of hair roots, and thus preserves the tissue surrounding the hair bulb.

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Market Info

Thinning hair/hair loss products represent 28% of all hair care treatments on the market

Prestige OTC anti-hair loss treatments are helping to modernise & bring credibility to the category. Brands are proposing new natural and high tech actives and targeting both men and women.

Schwarzkopf & Henkel - Hair Tonic for Women
to encourage hair growth and reduce normal hair loss. To strengthen and revitalise hair, and maintain the condition of the hair follicle.
Ing: carnitine , taurine, tataric acid, echinacea

Biotherm - Regenetic Anti-Hair Loss Serum
This product for men targets hair loss problems due to premature ageing of the hair follicle and the accumulation and rigidification of the collagen surrounding the root.
Ing: Aminexil®, thermal plankton, ceramide, carbocysteine

DHC – Medicated Hair Tonic
Work on hair growth by extension of the “anagen” stage.
Ing : mulberry root periderm extract

In today’s image-conscious society, people are looking for an affordable cosmetic hair loss solution that delivers on its promises. This presents an opportunity for high performance, clinically proven anti-hair loss…

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Hair Science

Hair appear much more complex that they look.

They are composed of 2 structures:

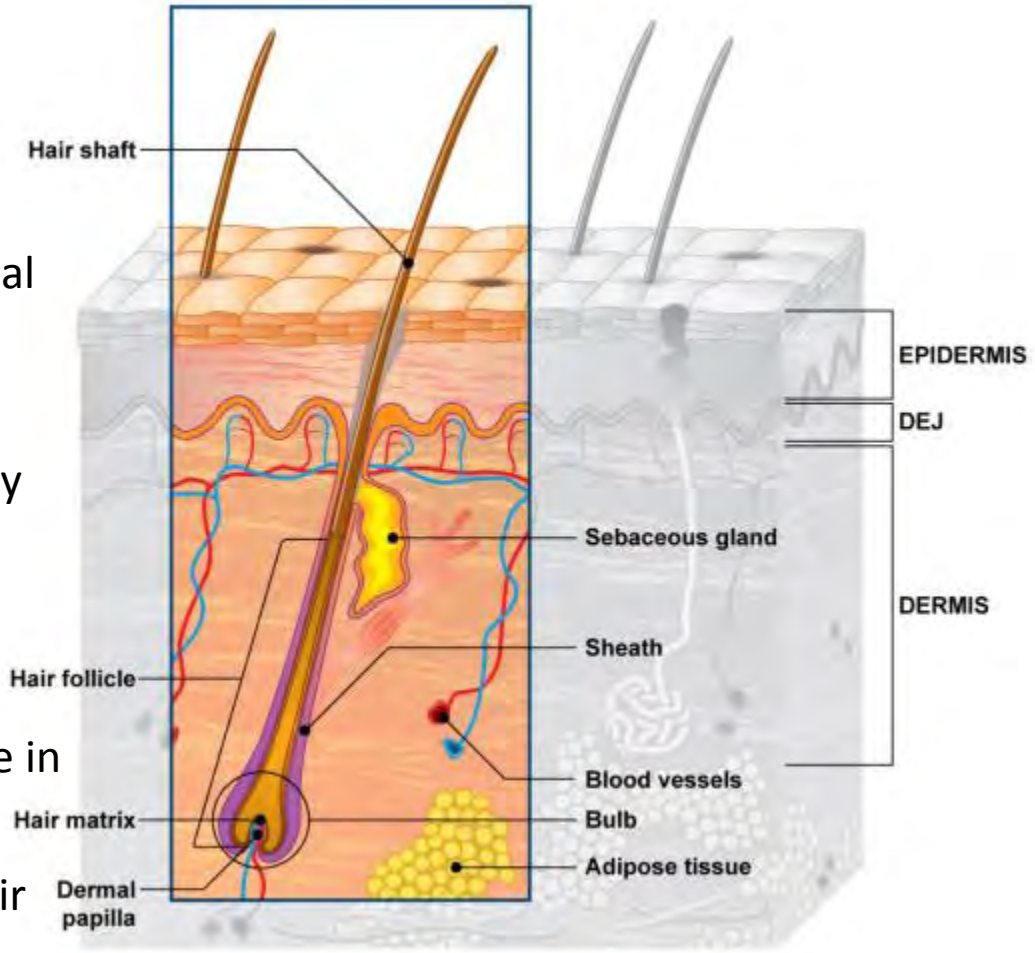
-Above the skin = ***hair shaft***

-Beneath the skin = ***hair follicle***

At the base of the follicle is the dermal papilla & ECM.

As papilla & ECM new cells grow, they push the previous cells upwards to form the hair.

The dermal papilla plays a crucial role in the dermal-epidermal interactions and is of great importance for the hair formation and growth cycle.



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Hair Science

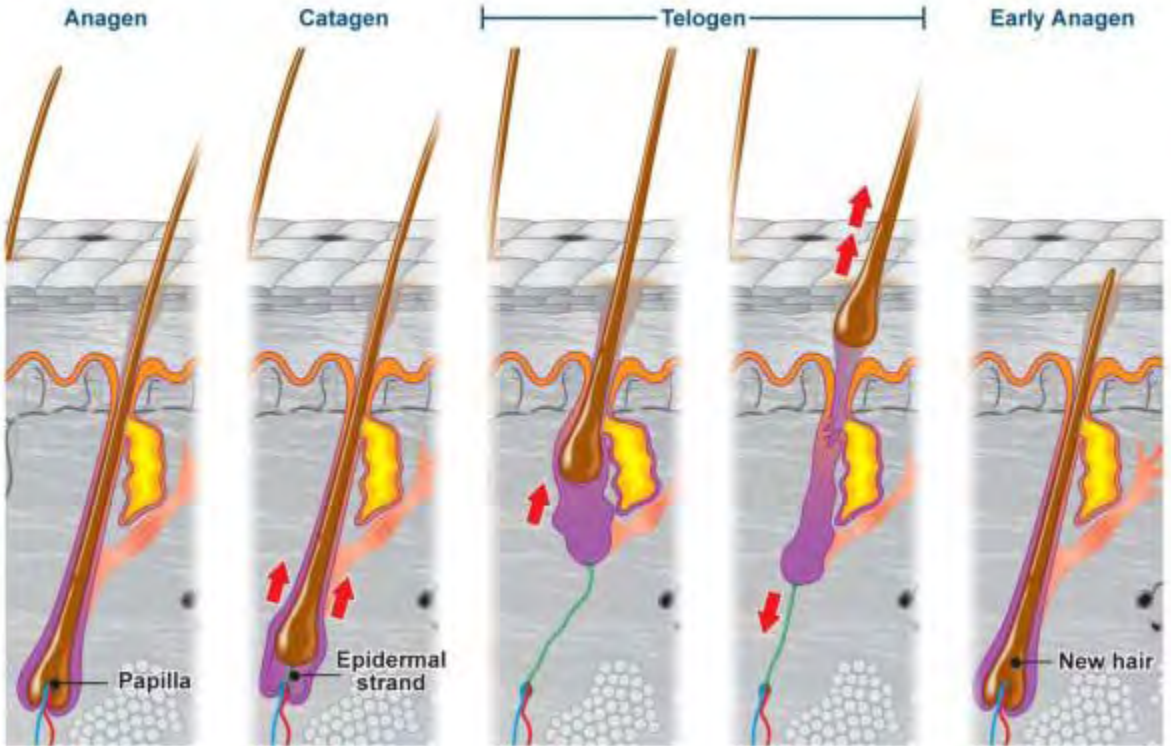
We carries ±100 000 hair follicles. Each follicle can grow many hairs over a lifetime (±20 times).

The hair follicle growth cycle has 3 distinct phases:

- **Anagen**: (Growth phase 70 – 85% hair). Hair are growing for 2- 6 years.

- **Catagen**: (Transition phase – 1-2%). The hair bulb separates from the dermal papilla, the hair follicle migrates toward the scalp and remain in this phase for 2-3 weeks.

-**Telogen**: (Resting phase – 100 days). Hair stay attached to the follicle and fall out to be replaced by the next hair in anagen phase (papilla & follicle join together again & new hair begins to form).



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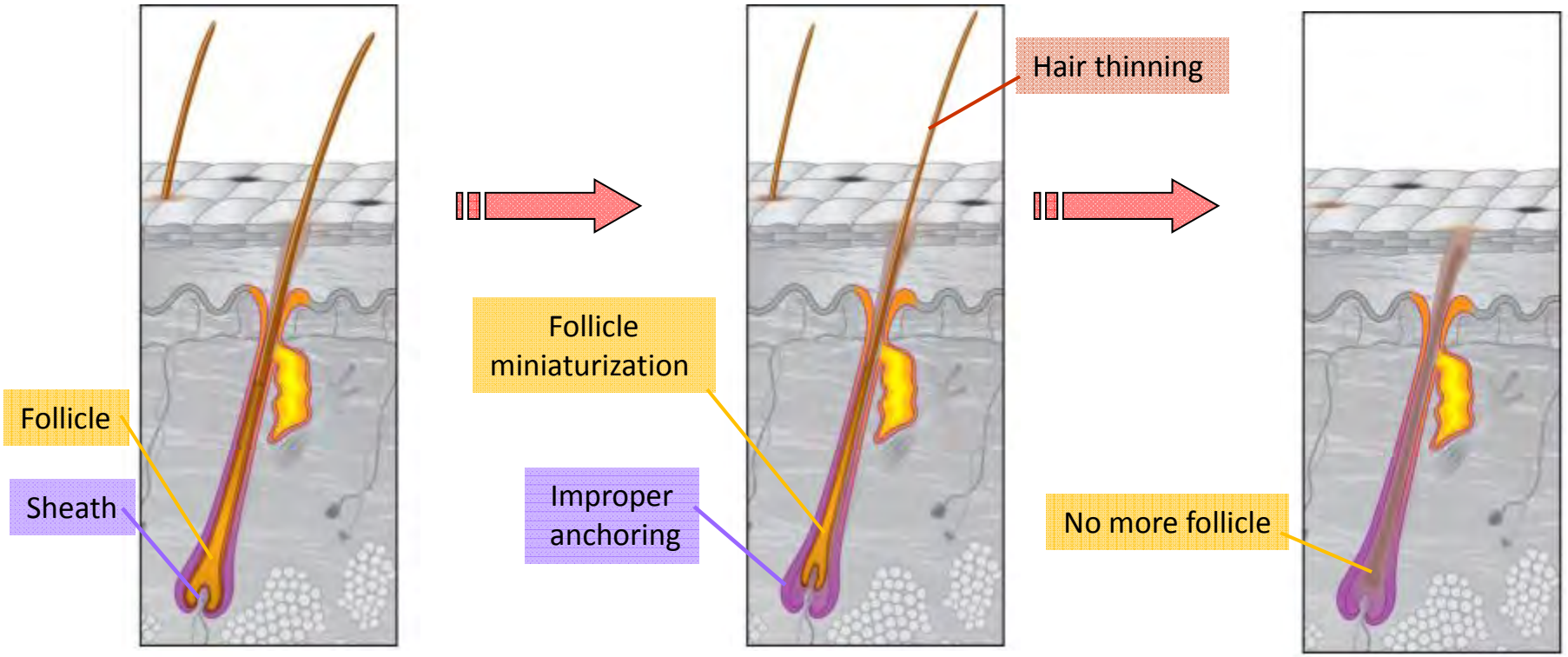
Hair Loss: How it works?

Normal hair growth cycle

Altered hair growth cycle (↓ Anagen + ↑ Telogen)

Hair loss



- No hormonal dysfunction
- ECM proteins integrity
- No inflammation

- ↑ DHT : shorthens Anagen phase → Miniaturization of follicles
- Loss of ECM proteins renewal → Follicle size reduction & loss of hair anchoring
- Inflammation → Disruption of hair cycle

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Mechanism of action in details:

-DHT Modulation
-ECM Integrity
-Inflammation

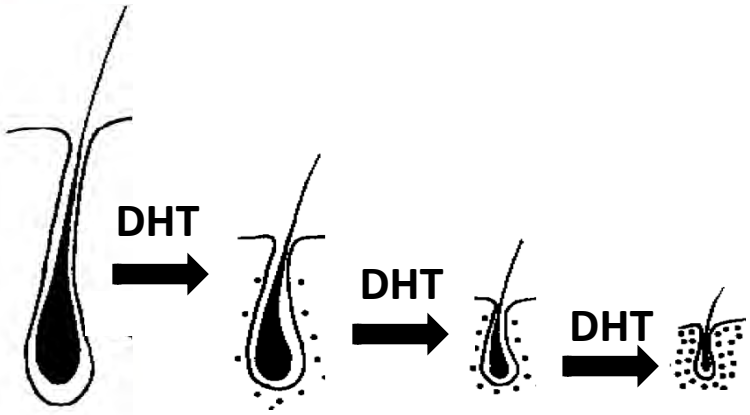
Effect of Dihydrotestoterone (DHT)

DHT is formed by the action of the enzyme 5-α-reductase on testosterone. DHT causes hair loss by shortening the growth phase of the hair cycle, causing miniaturization (decreased size) of the follicles, and producing progressively shorter and finer hairs.

5-α-reductase participates in metabolic pathways: bile acid synthesis, androgen and estrogen metabolism, prostate cancer & acne

5-α reductase

Testosterone → **DHT (dihydrotestosterone)**



DHT shortens the hair growth cycle (shorter anagen phase)

↓

Miniaturization of the follicles

↓

Producing progressively shorter, finer hairs

↓

Hair loss

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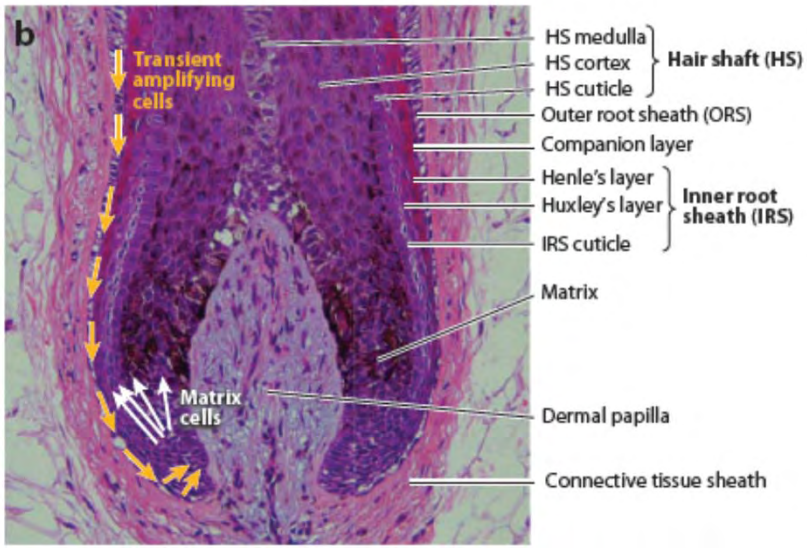
Effect of Loss of ECM integrity

Hair follicles size is determined by:

-the volume of its **dermal papilla**
-the volume of **the extracellular matrix**



Healthy dermal papilla will produce good ECM proteins such as **collagen type III** and anchoring fibers such as **laminin** and **collagen VII** which **will favor a good hair anchoring in the bulb surrounding tissue**.

If improper ECM renewal, hair will eventually **lack vigor** and will **thin**.

Cycle after cycle, the follicle becomes **smaller** and finally**, miniaturized and fall**.

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Effect of Inflammation

Androgenetic alopecia (AGA)

Hormones (DHT)

Chemicals

Climatic variations

Stresses (internal / external)

Aging

Production of pro-inflammatory cytokines

Alteration of the ECM

Hair follicle degradation

HAIR LOSS

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Focus on Capixyl™

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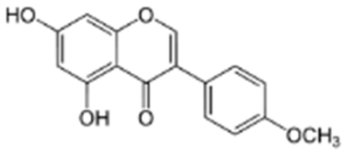
Capixyl™: Unique anti-hair loss combination

Biochanin A extracted from Red clover

Biochanin A is a powerful isoflavone



Red clover (*Trifolium pretense*) was traditionally used to treat asthma, cancer and inflammatory skin disorders such as eczema & psoriasis.

Biochanin A is an **effective inhibitor of 5-α-reductase (type I & II)** activity, thus modulating the conversion of testosterone to DHT in androgenic alopecia.

Acetyl tetrapeptide-3

4 amino acids biomimetic peptide derived from a signal peptide which stimulates tissue remodeling.

The peptide has a direct effect on hair follicle. The remodeling signal will increase the size of hair follicle for **better hair anchoring** and vitality.

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A clinically proven anti-hair loss active!!!

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Clinical study on hair loss

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Clinical Efficacy on Hair Loss

Test Protocol

- **30 volunteers** with **androgenetic alopecia (average age 46)**

  no iron deficiency anemia, no thyroid related conditions or any other possible pathology

  Must had 200 hair on the treated zone & 70% in anagen phase

- 15 treated with the **Capixyl™ lotion** (5%) and 15 with a **placebo**

  Formulation composed of water 75% and alcohol 20%

- Once a day application at night time of 20 drops of the **Capixyl™ leave-on lotion** or **placebo** for a period of **4 months**

- A **digital trichogram** (TrichoScan professional) was taken at D0 and 4 Months.

  - Quantification of number & the growth of hair in anagen & telogen phases

  - Quantification of the variation of number of hair after 4 months

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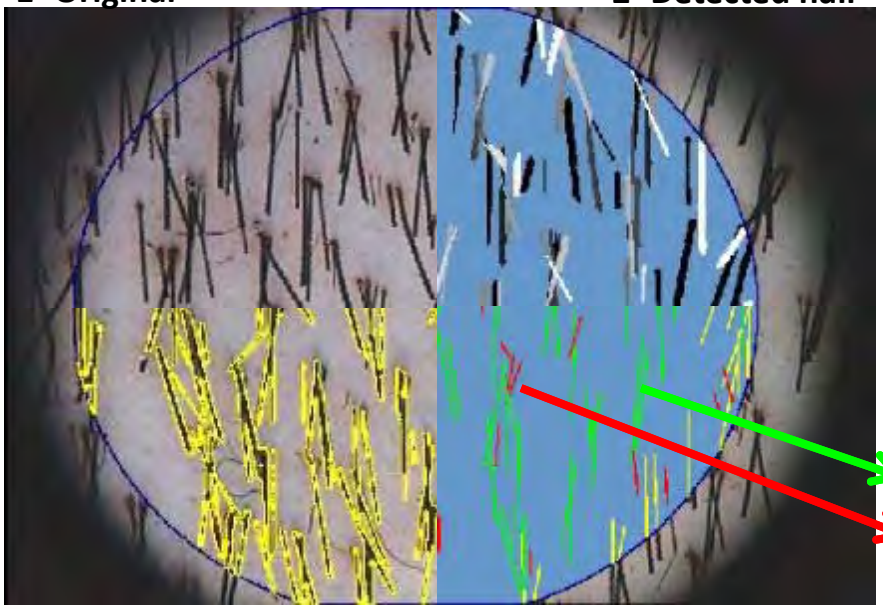
How to perform TrichoScan

1. Hair **shaving** (~ 1.8 cm^2 areas)

2. Take a **picture** of the aera zones 3 days after shaving (to evaluate the anagen and telogen phases).
   Anagen phase was determined as a growth rate of 0.3 mm/day.

3. Results analysis by microscopy & automatic digital image analysis

1- Original **2- Detected hair**



3- Marked hair **4- Anagen/Telogen hair**

Green : Anagen
Red : Telogen

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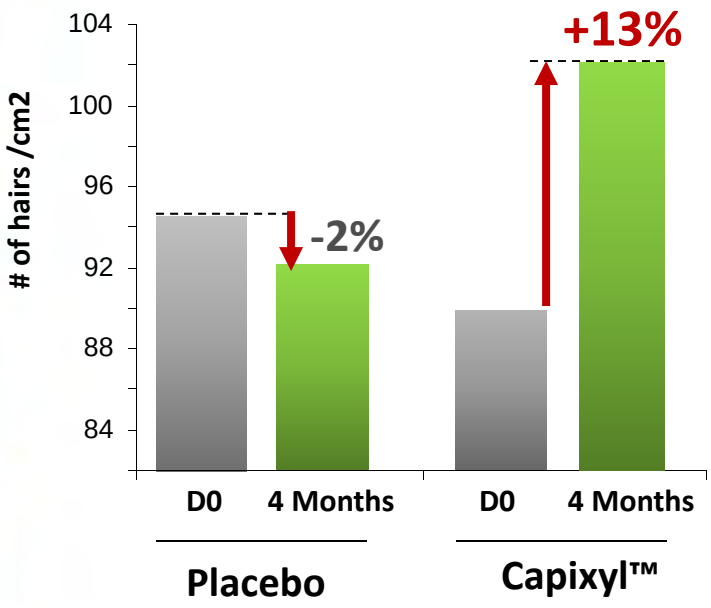
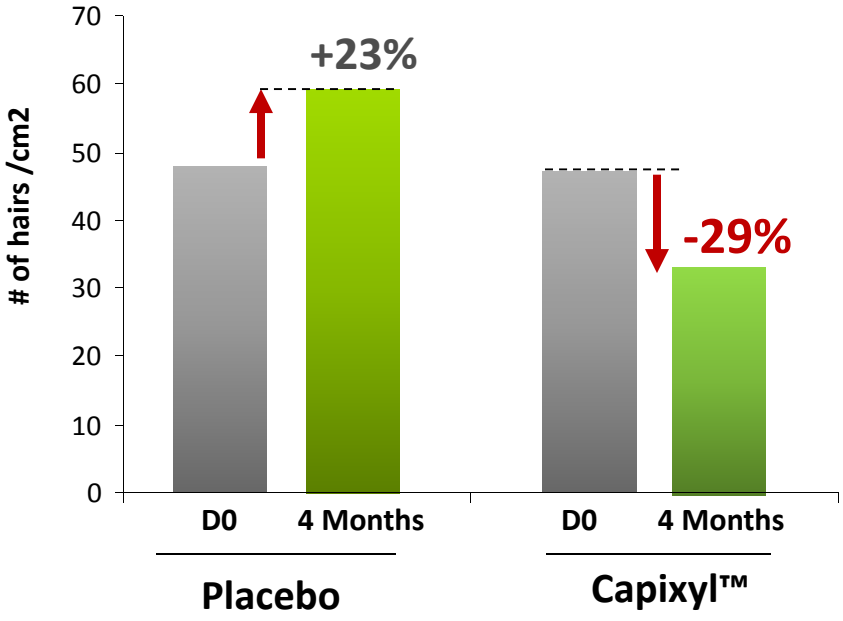
Results: Anagen and Telogen hair density

Average Anagen (Growth) hair density



Average Telogen (Fall) hair density

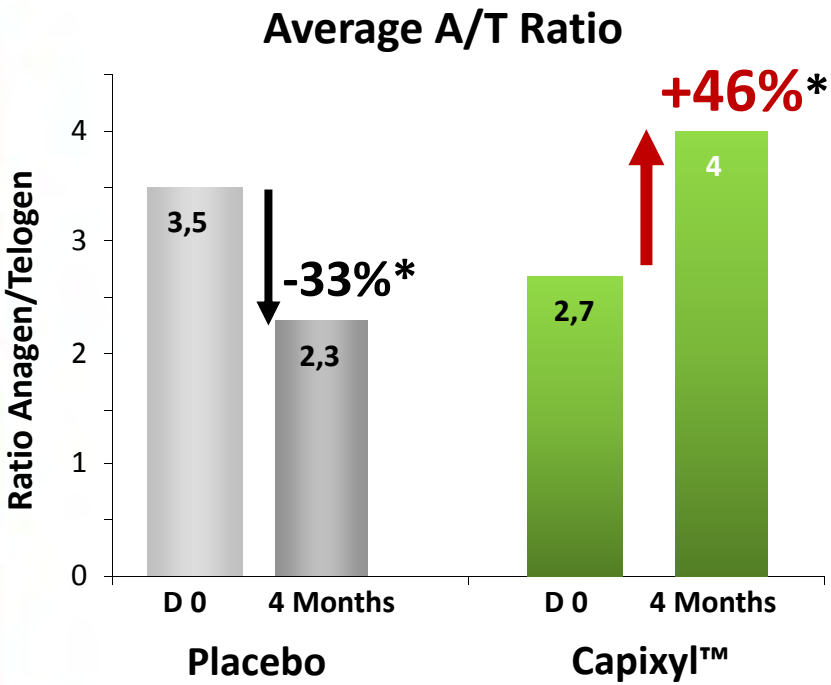


More than 70% of the volunteers saw an improvement in their condition

Capixyl™ induces a clear increase in the anagen hair density = HAIR GROWTH
Capixyl™ induces a strong reduction in the telogen hair density = STOPS HAIR LOSS

Results: Ratio Anagen / Telogen

A/T= Comparison of the number of anagen and telogen hair, which is an indication of the percentage of active hair follicles



↑ A/T ratio = activation of hair growth

→ **Treatment is working!**

Hair loss stops!

↓ A/T ratio = loss of hair growth activity

→ **Alopecia continues / worsens**

* P ≤ 0.05

Capixyl™ increases the A/T ratio of 46% compared to a reduction of -33% for the placebo attesting the efficacy for stimulating hair growth and reducing hair loss

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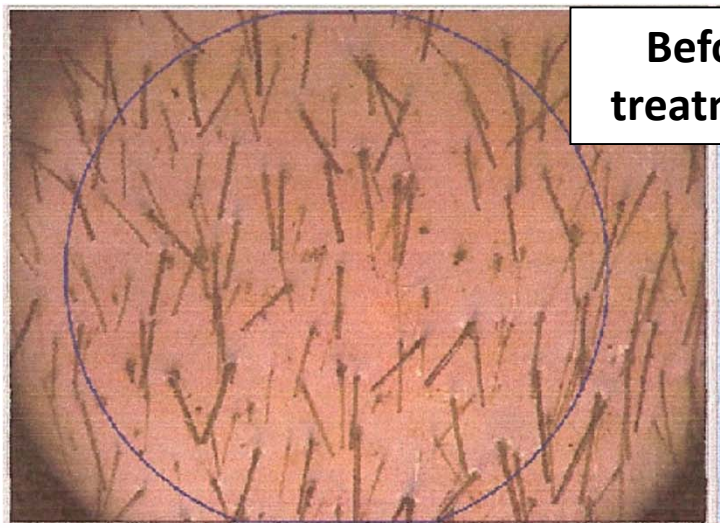
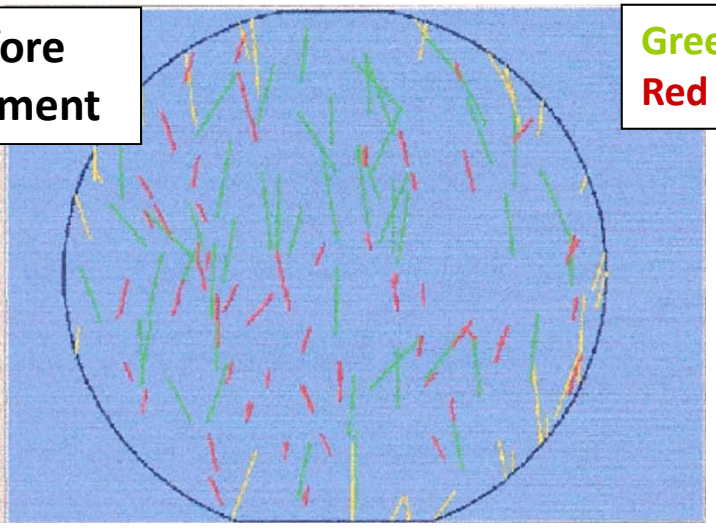
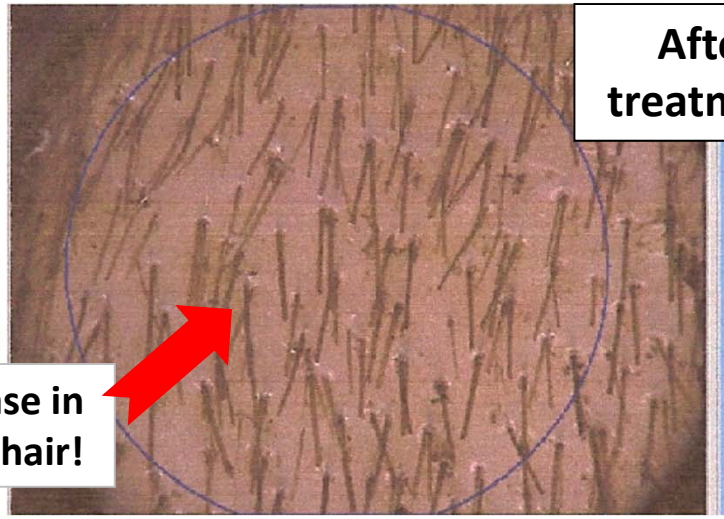
Before & After Pictures



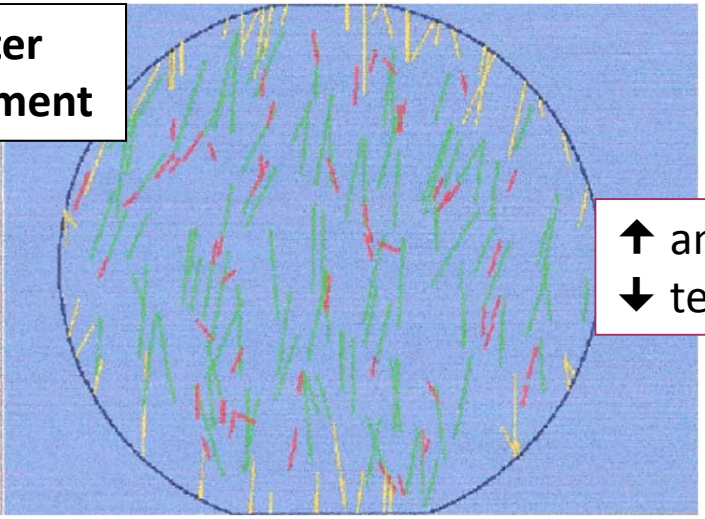
Before treatment



Green anagen
Red : telogen



After treatment



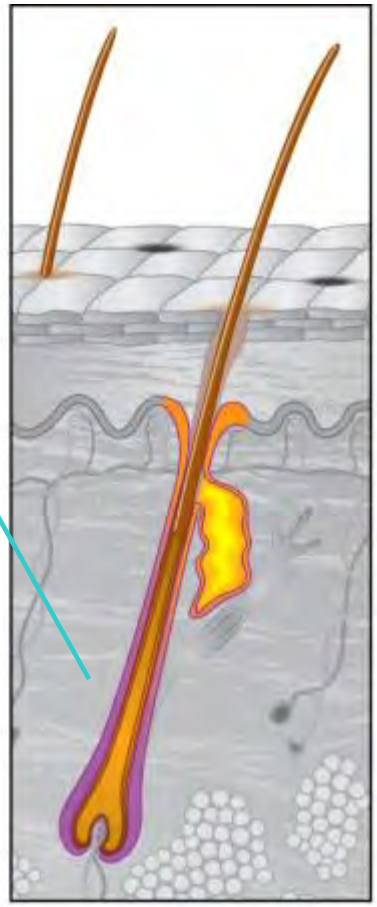
↑ anagen hair
↓ telogen hair

Clear increase in number of hair!

Capixyl™ is an efficient active to decrease alopecia

In Vitro Effect of Capixyl™ on Inflammation

Inflammation Reduction
IL-8 reduction



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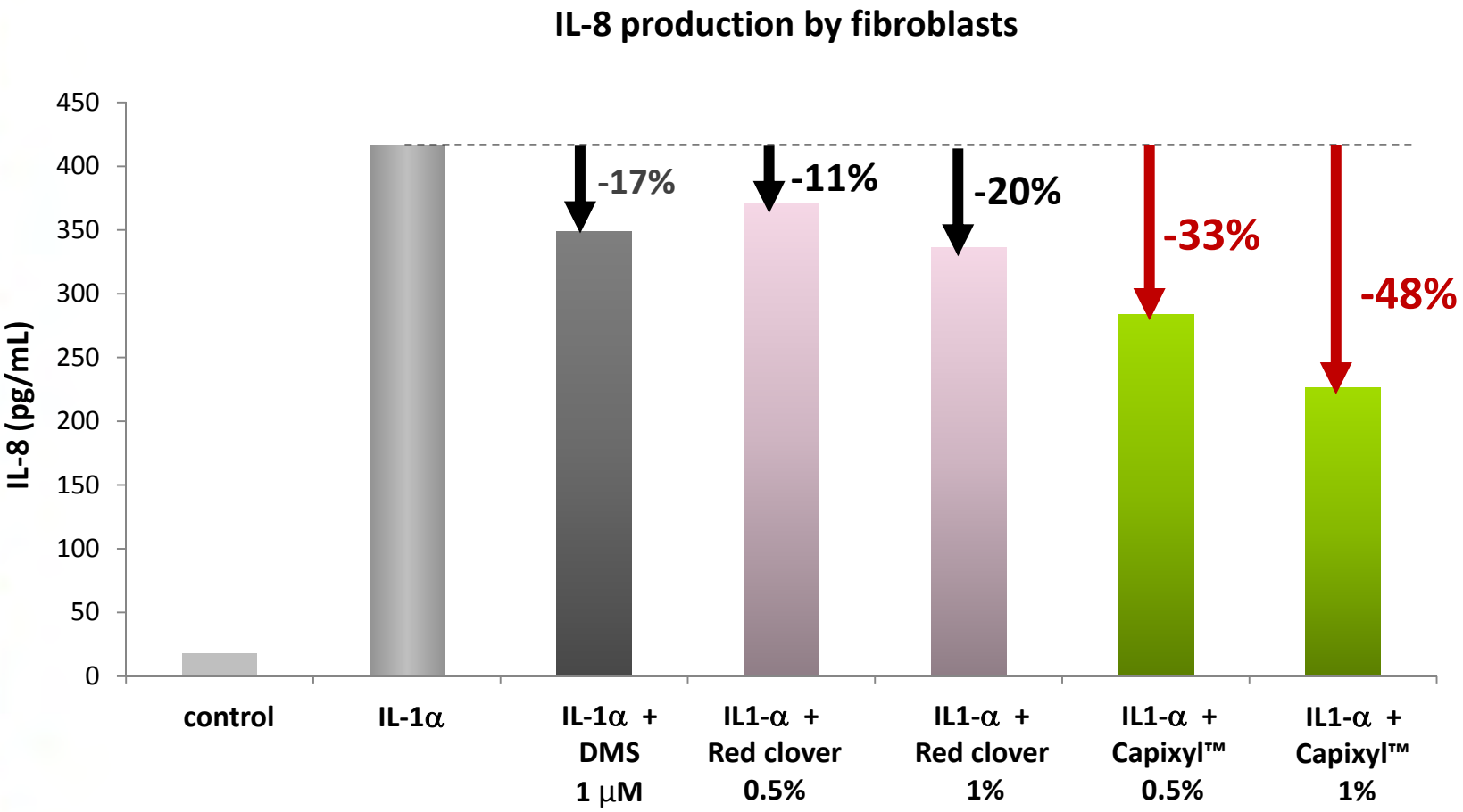
Effect of Capixyl™ on IL-8 production



Capixyl™ decreases pro-inflammatory cytokines with a synergistic action compared to red clover extract alone

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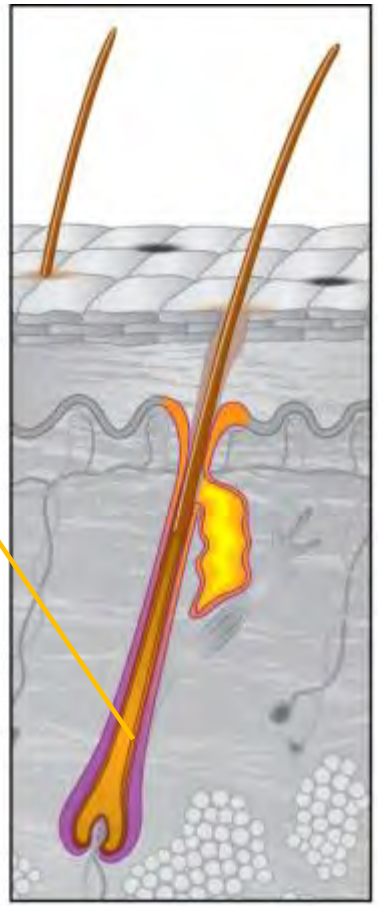
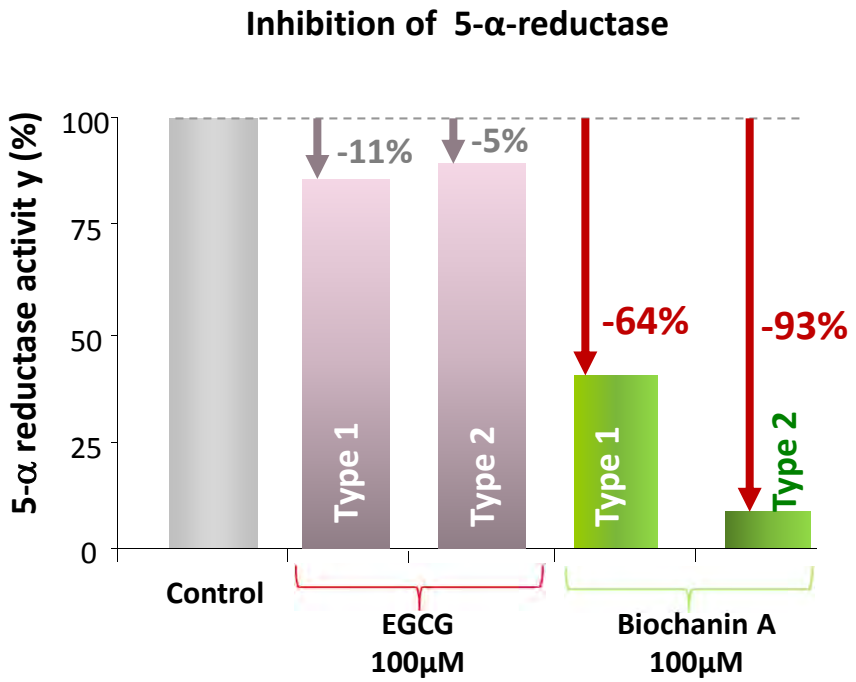
In Vitro Effect of Biochanin A on 5-α reductase

DHT modulation
Via 5-α reductase inhibition
by Biochanin A
in the red clover extract



UNIPEX

Effect of Biochanin A on 5-α reductase activity



Biochanin A inhibits 5-α reductase activity, thus confirming its effect on DHT production to reduce androgenic alopecia.

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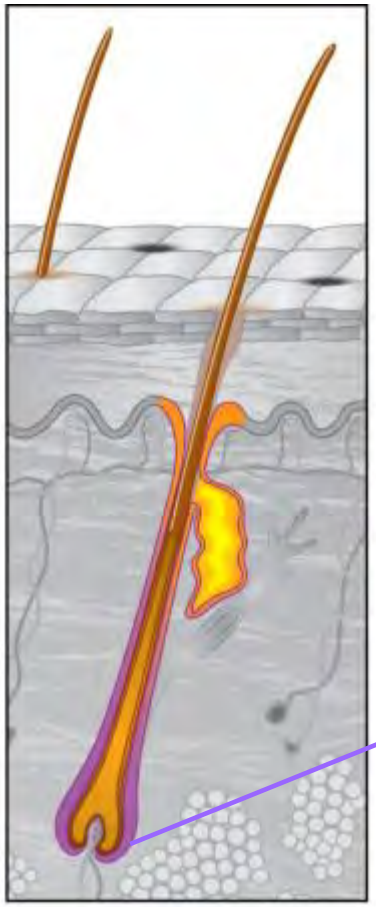
In Vitro Effect of the Peptide on anchoring proteins



Follicle ECM renewal &
Stimulation of anchoring proteins
Stimulation of collagen,
Collagen III,
Collagen VII and Laminin
by Acetyl tetrapeptide-3

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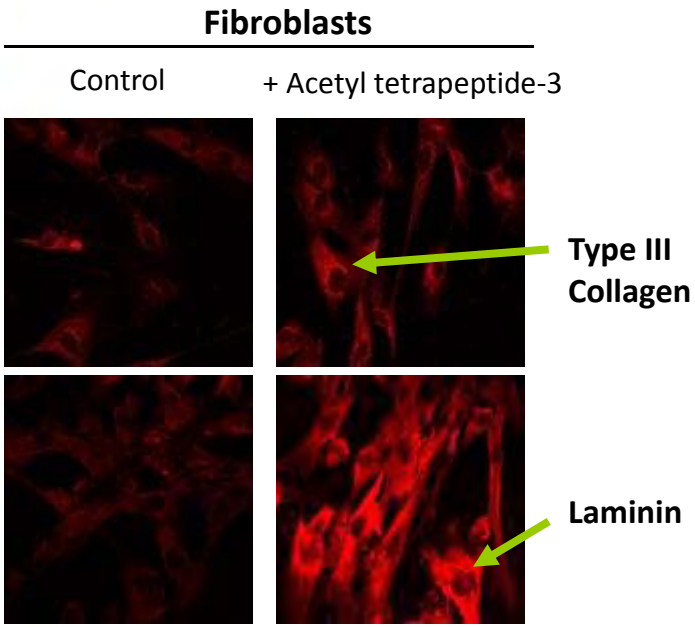
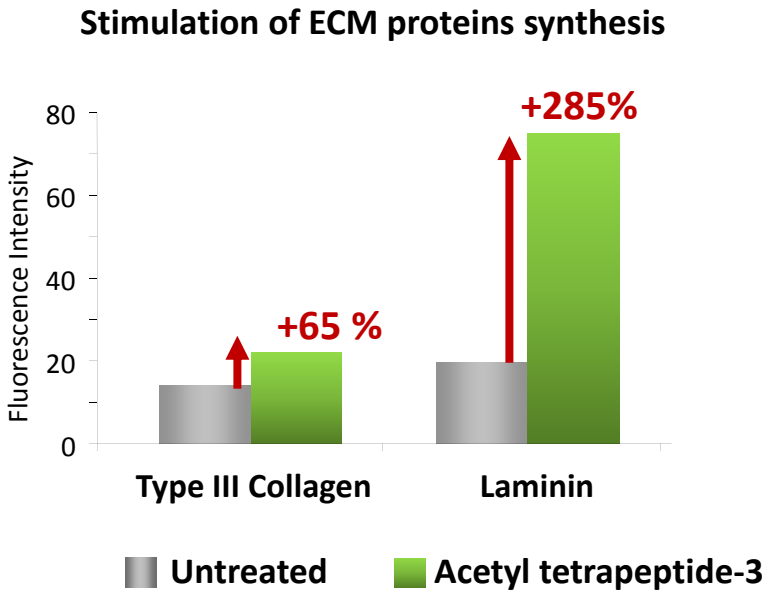
Acetyl tetrapeptide-3 & Proteins synthesis



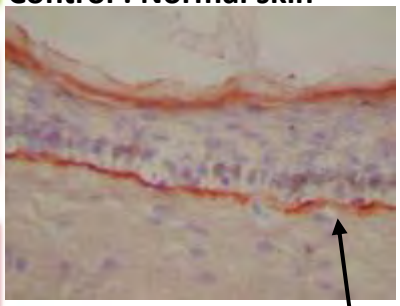


Acetyl tetrapeptide-3 induces the synthesis of laminin, type III collagen in fibroblasts

Acetyl-tetrapeptide-3 stimulates dermal papilla extracellular matrix proteins thus having a direct effect on hair follicle size and better anchoring

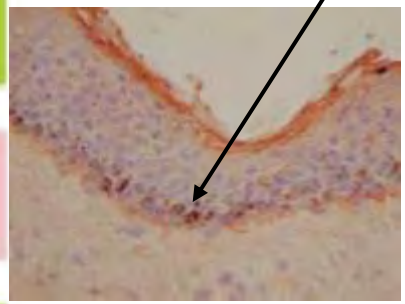
Acetyl tetrapeptide-3 & collagen VII synthesis

Control : Normal skin

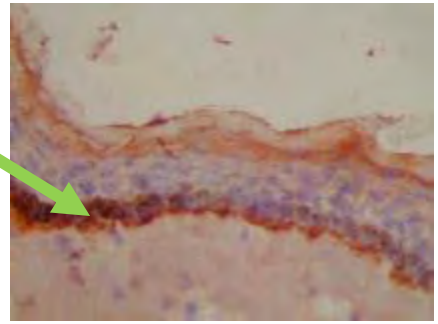


Collagen VII

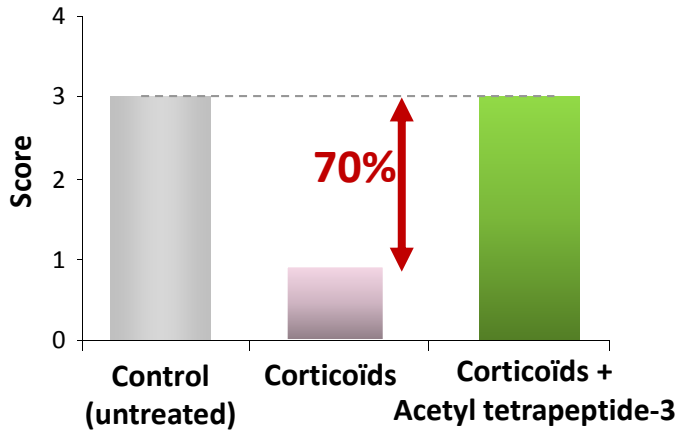
Skin + Corticoïds



Skin + Corticoïds + Acetyl tetrapeptide-3



Evaluation of Collagen VII



Acetyl tetrapeptide-3 provides a repairing effect at the dermal-epidermal junction level, improving hair anchoring

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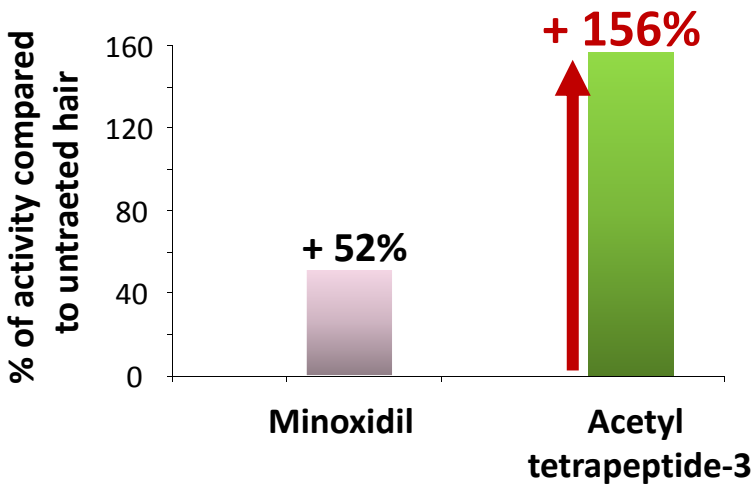
Ex vivo: Comparative study with Minoxidil

Hair growth activity of the treatment compared to untreated hair



Acetyl tetrapeptide-3 stimulates hair growth with higher activity than the reference hair growth product, Minoxidil

New Clinical Results

UNI-PEX

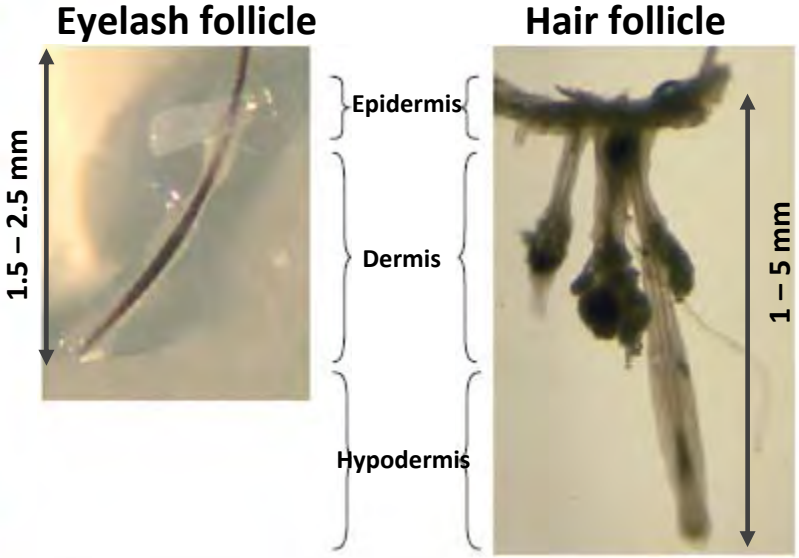
Hair and lash similarities

Upper lid: Number :100-200 ; length: 8-12 mm

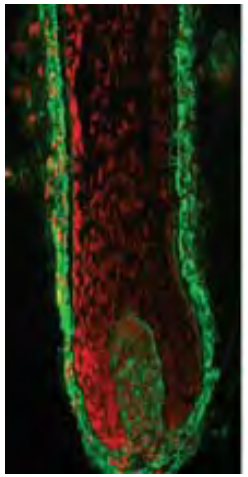
Lower lid: Number :75-100; length: 6 to 8 mm

Compared with scalp , eyelid revealed a thinner epidermis and no hypodermis.

Eyelash follicles has the same overall structure as scalp hair follicles, but much shorter (due to a shorter hair cycle).



Specific labeling with ECM proteins antibodies revealed a similar morphology to that observed in the scalp hair follicle



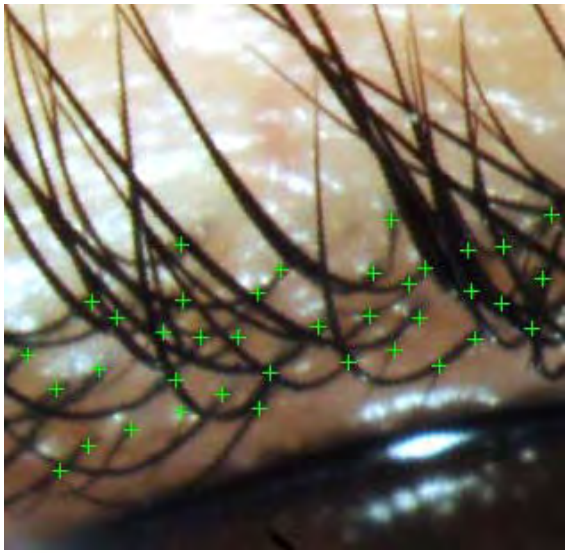
After 40 years old, the number of eyelashes decreases and they become thinner

Evaluation of the lash density

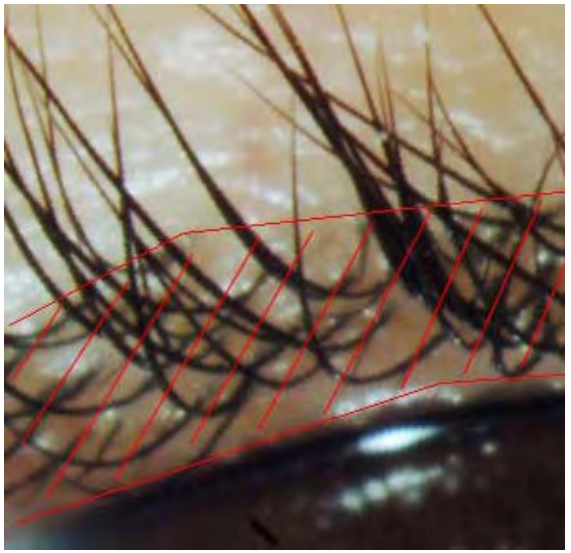
Lash density : number of roots per unit of surface

1 - At D0, 4 weeks and 8 weeks, photographs of the upper lashes were taken with a camera fixed on a biomicroscope

2 - Counting the number of lashes in the specific area to be analyzed



3 - Measurement of the surface where the lashes growth



4 - Determination of the lash density

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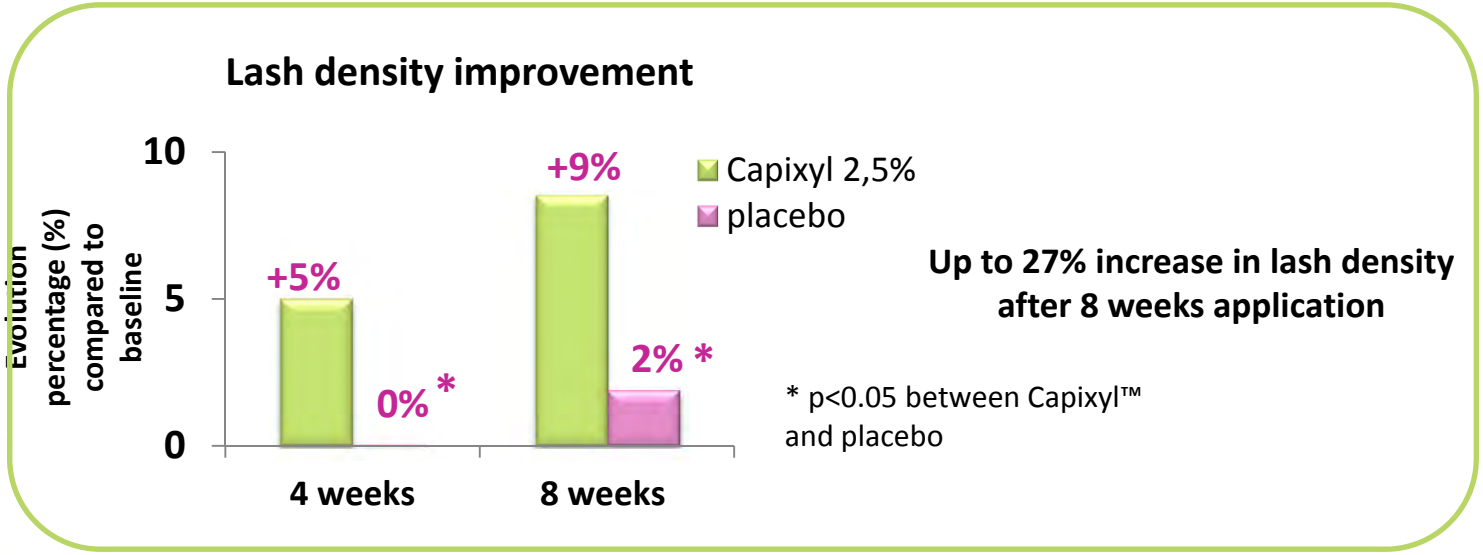
Evaluation of the lash density



After 4 weeks 73% of the subjects improved in lash density and 93% had an effect after 8 weeks

Vol #14

T0

T 8 weeks

Capixyl™ induces a clear and significant increase in the lash density (increase in new lashes & decrease in falling lashes)

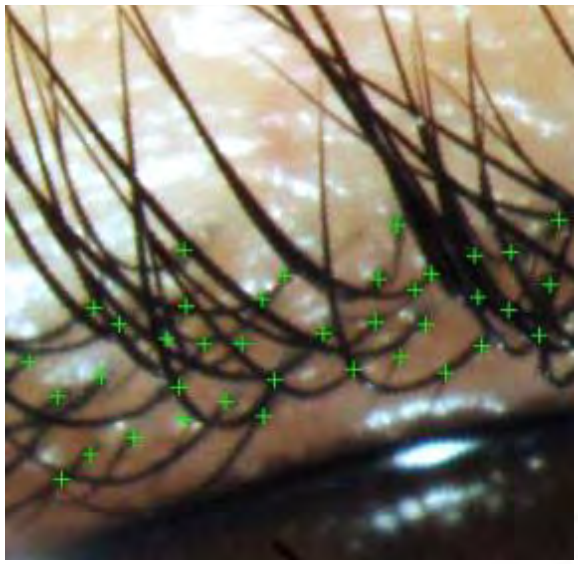
Evaluation of the number of new lashes

Characteristics of young lashes (in comparison with adult lashes):

- less coloring
- thinner
- shorter

1 - At D0, 4 weeks and 8 weeks, photographs of the upper lashes were taken with a camera fixed on a biomicroscope

2 - Counting the number of new lashes according the morphology and characteristics of young lashes.



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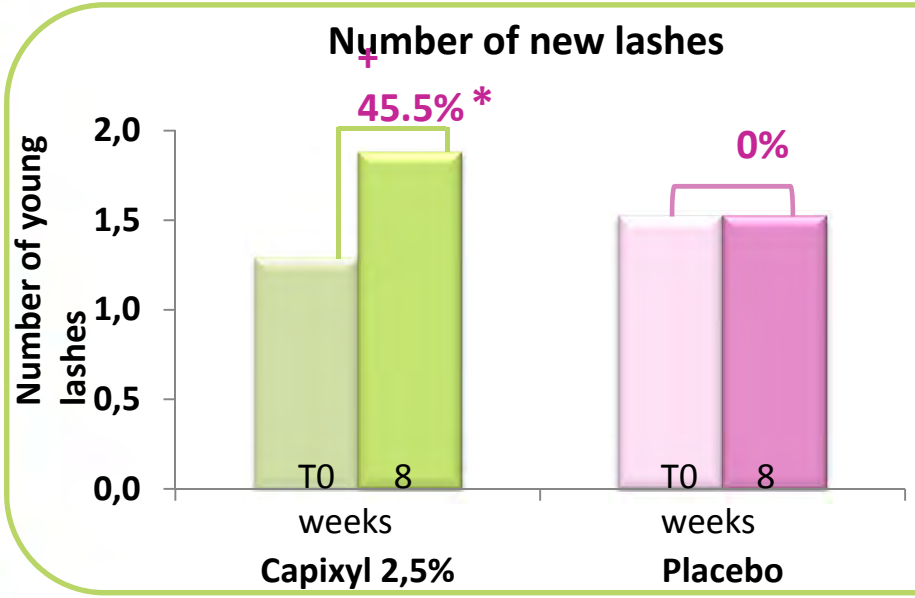
Evaluation of the number of new lashes



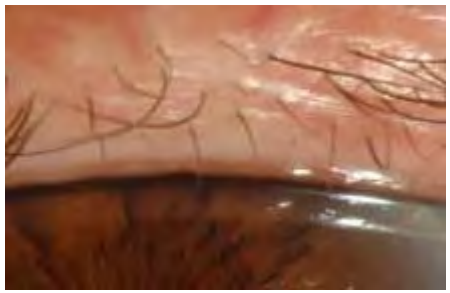
Number of new lashes improves significantly by 45.5% after 8 weeks application

No visible effect with placebo

* p<0.1 between 8 weeks and T0

Vol #10

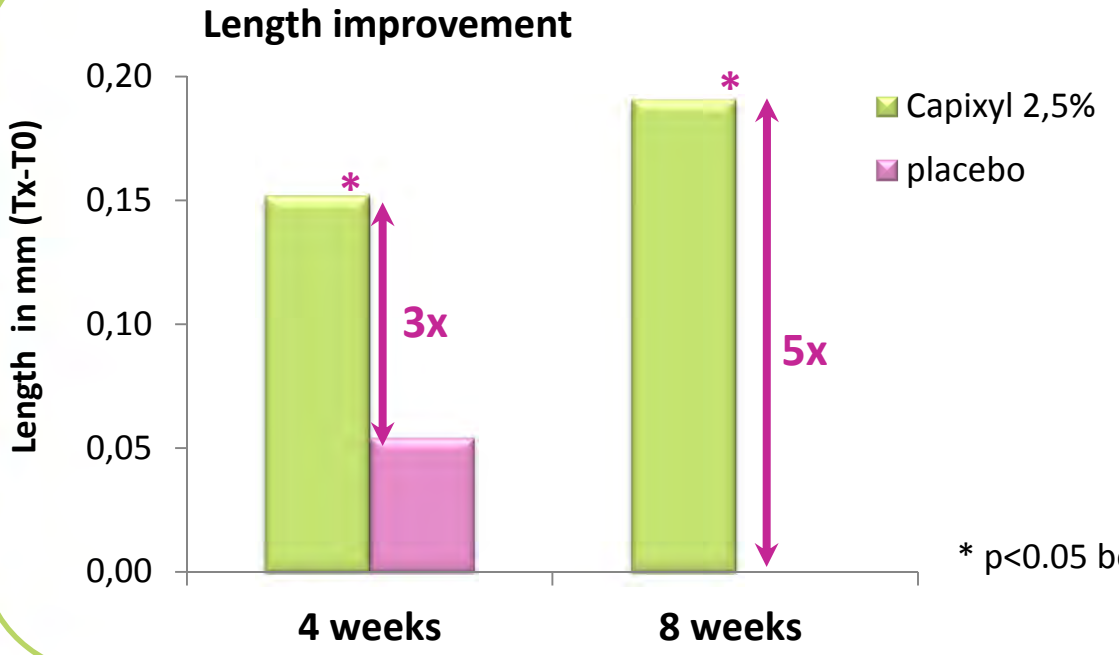
T 4 weeks



T 8 weeks

Capixyl™ significantly increases the number of new lashes after 8 weeks application

Evaluation of the lash length



The evolution of lash length is 3 and 5 times better after Capixyl™ application (4 and 8 weeks respectively) in comparison with placebo

* p<0.05 between 4 or 8 weeks and T0

After 8 weeks 73% of the subjects saw an improvement in the length of their lashes

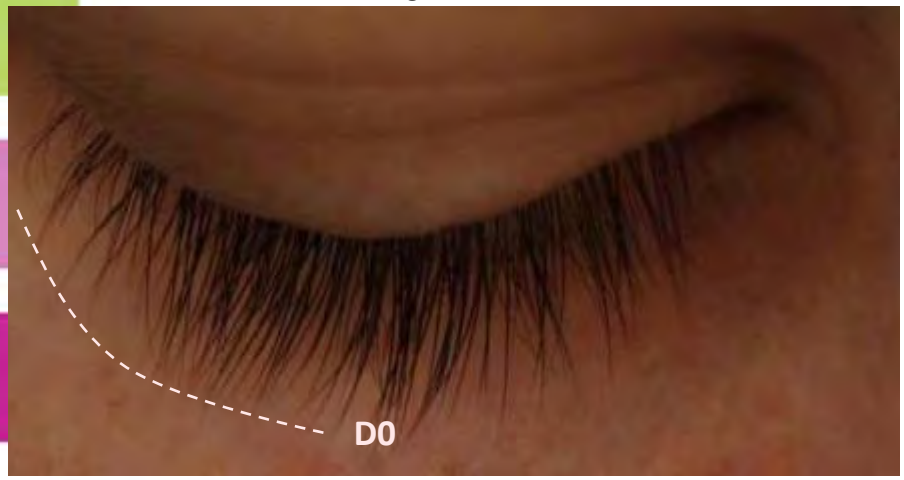
Up to 0.70 mm growth after 4 weeks

Capixyl™ improves significantly lash growth after only 4 weeks application

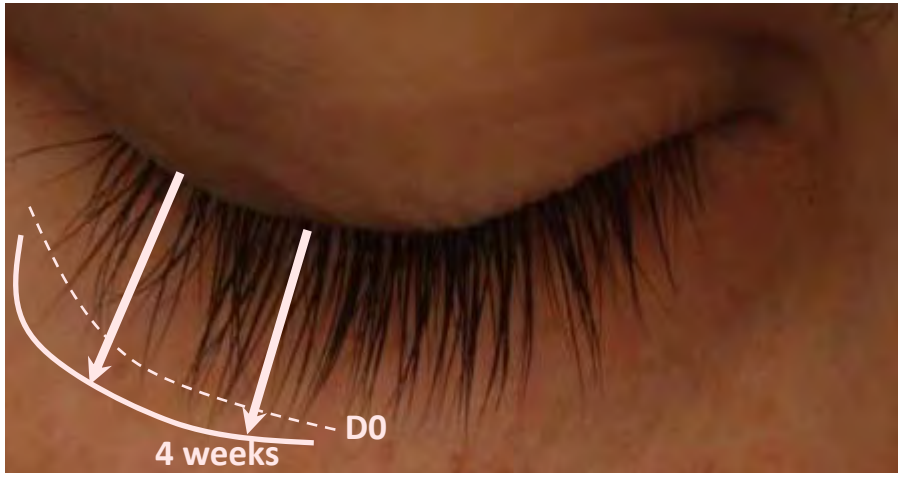
Evaluation of the lash length

Vol #3

T0

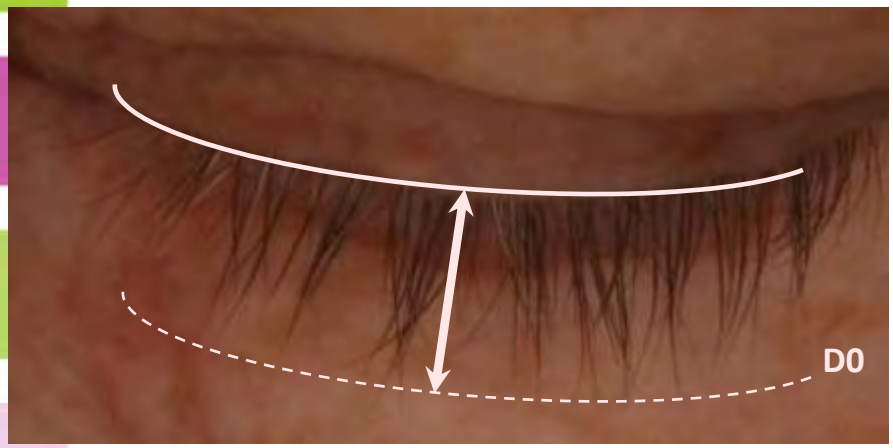


T 4 weeks

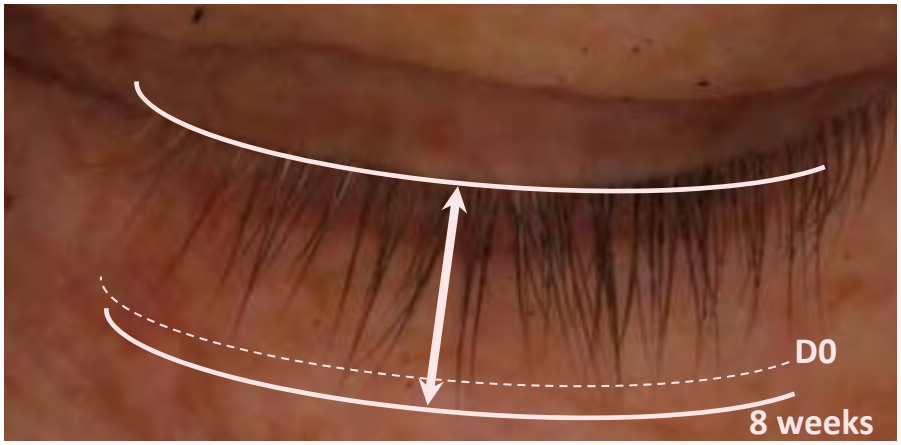


Vol #2

T0



T 8 weeks



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Evaluation of the lash length

Vol #16

T0 | T 4 weeks | T 8 weeks

Up to 0.70 mm growth after 4 weeks

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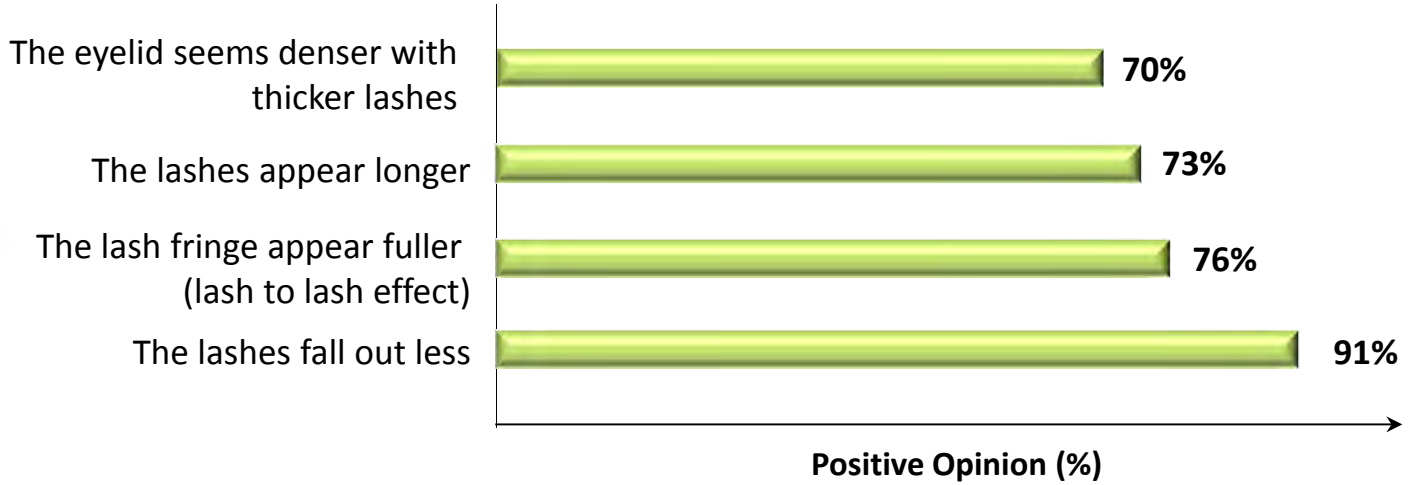
Consumer Evaluation



Consumers noticed a real improvement when they used Capixyl™ in an eyelash treatment

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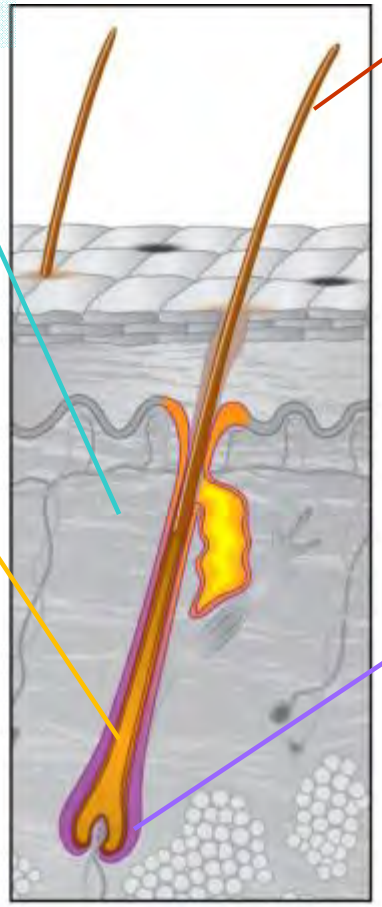
Capixyl™ Efficacy summary

Inflammation Reduction
IL-8 reduction by Capixyl™

Stop hair loss & Hair growth stimulation
Clinical & *ex vivo* Comparative study with Minoxidil

DHT modulation
5-α reductase inhibition by Biochanin A



Follicle ECM renewal & Stimulation of anchoring proteins
Stimulation of collagen, Collagen III, Collagen VII and Laminin by Acetyl tetrapeptide-3

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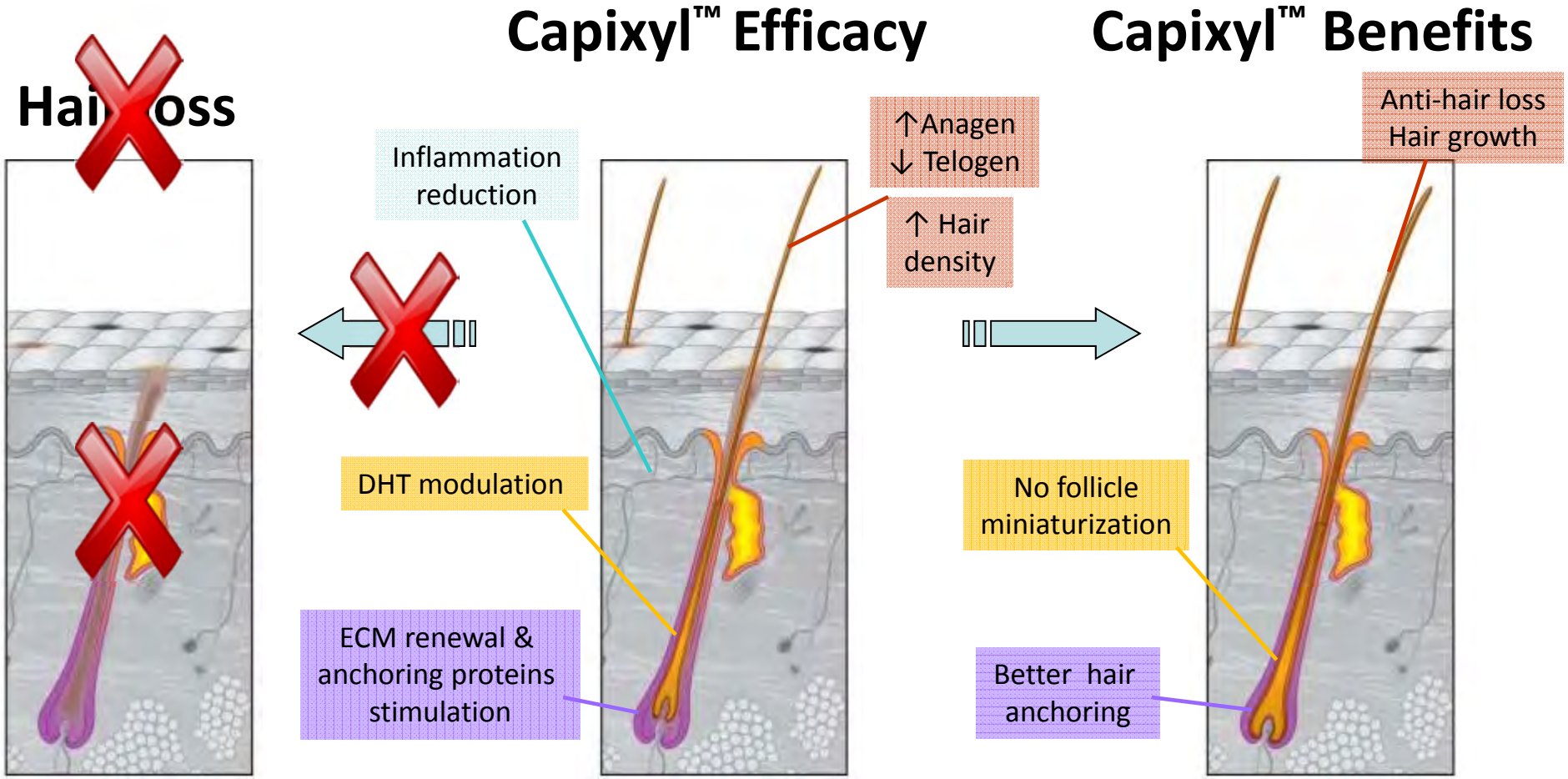
Capixyl™ Summary



- Inhibition of 5α-reductase, thereby modulating the conversion of testosterone to DHT → No miniaturization of follicles
- ECM proteins renewal → Better hair anchoring
- Inflammation reduction → Normal hair cycle

Tolerance Studies

- Ocular tolerance (HET CAM) (tested at 15%)
- Acute skin tolerance (single patch test) (tested at 25%)
- HRIPT (irritation and sensitization on 100 volunteers) (tested at 15%)
- Mutagenic Potential In Vitro Test – AMES TEST (tested at 25%)
- In vitro 3T3 phototoxicity (tested at 15%)

Excellent Safety Profile

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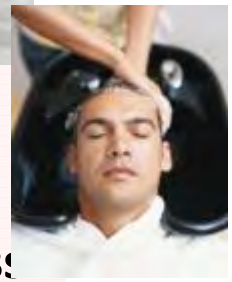
Applications

Recommended dosage:

- Intensive treatment: 5%
- Preventive care: 0.5 – 2.5%



Potential Applications:

- **Anti-hair loss**
- **Hair regrowth**
- **Eye lashes**
- **Leave-on**
- **Hair treatment for menopaused women**
- **Scalp treatment**
- **Lotions**
- **Tonics**
- **Anti-aging hair care prod**
- **Treatment for seasonal h** **ss**
- **Eyelash mascara**
- **Eyelash serum**
- **Eyelash conditioner**
- **Eyelash treatment**
- **Active makeup**

Incorporation: at the end of the formulation (< 40˚C), pH:4-8

INCI name: Water (and) Butylene Glycol (and) Dextran (and) Acetyl tetrapeptide-3 (and) Trifolium Pratense (clover) Flower Extract

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Formulation Tips

Capixyl™ is an clear aqueous solution easy to work and formulate with.

Capixyl™ should be added in the cooling phase at the end of the formulating process.

Very good solubilisation in water.

Presence of alcohol allows the active to have a better penetration in the scalp.
Presence of preservative is not necessary with 20% and more alcohol.

Should used a buffer before adding the active.

No known incompatibilities.

pH: 4 – 8

Phase	Coomercial name	Supplier	INCI Name	%
A	Water	-	Aqua	qsp
	Sodium Phosphate	Acros	Sodium Phosphate	1,117
	Citric Acid	Interchimie	Citric Acid	0,715
B	Tinogard Q	Ciba	Tri(Tetramethylhydroxypiperidinol) Citrate	0,025
	UCON 50-HB-3520	Unipex / Dow	PPG-28-Buteth-35	0,50
	Mirasil DMCO	Unipex / Bluestar	PEG/PPG - 22/24 Dimethicone	0,50
	Capixyl™	Unipex	Water (and) Butylene Glycol (and) Dextran (and) Acetyl Tetrapeptide-3 (and) Trifolium Pratense (Clover) Flower Extract	5,00
	Ethanol	-	Denaturated Alcohol	20,00
C	Eumulgin HPS	Cognis	Ceteth-7 (and) PPG-1-PEG-9 Lauryl Glycol Ether (and) PEG-40 Hydrogensted Castor Oil	0,60
	Parfum Neva	Cinquième Sens / Floressence	Parfum	0,10

Mixing Procedure

1. Solubilize Sodium Phosphate in water, after complete solubilization, add citric acid.
2. One phase A is homogenous, introduce Phase B ingredients one at the time (in indicated order) and homogenize after each ingredient addition.
3. Mixed the solubilisant with the fragarance and then slowly add this pre-mix to the mix (phase A & B).. (NB : the fragrance pre-mix should be completly transparent before introducing it into the mix).
4. Check pH.

Caractéristiques

Aspect : Clear solution
pH = 5,50 – 5,70
Stability : 1 month at 45°C / 3 month at 40°C

Features & Benefits

Features	Benefits
Unique combinaision: Peptide with botanical active	**Stable, easy to work with**
3 different mechanisms of action	**Acts on most parameters influencing hair loss (reduce quantity of active in final product)**
Better efficacy than Minoxidil on hair growth	**Provides faster results without side effect**
High efficacy on hair growth	**Low dosage (starting at 0.5%) and fast action**
Clinical efficacy on hair loss	**Reverse the hair loss process and helps hair regrow after 4 months**

To focus on…

Innovations – Performance – Safety

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Summary

- **Capixyl™**: Innovative and unique anti-hair loss active.
- Effective combination of a signal peptide & red clover extract.
- **Complete** action on **hair loss causes**!
- Better than Minoxidil.
- Outstanding clinical results.
- Excellent safety profile.

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THANK YOU!

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