



CAPIXYL™

HAIR FERTILIZER



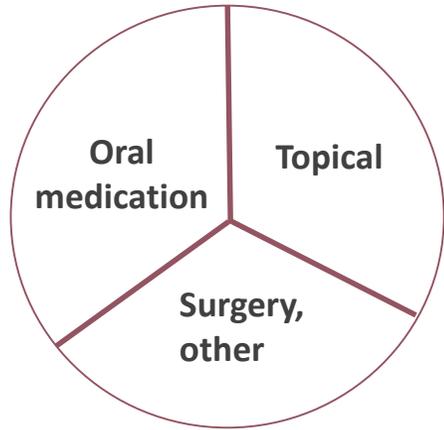
HAIR LOSS GENERALITIES

- Humans have +/- **100 000 hairs** on scalp.
 - A daily loss of 40 to 100 hairs is normal (up to 175 during season changes - autumn and spring)
 - Alopecia = daily loss >100 hairs during a long period (app. 2 months).
- **Main Cause of hair loss:**
 - Genetics
 - Hormonal change or imbalance (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 higher degree of hair loss (notably around the temples and the vertex) than women, but following menopause it may affect 75% of women older than 65 years old.



MARKET INFO

Global anti-hair loss market 2015 = 7.2 billions USD
expected to exceed USD 10 billions by 2024 => +4%/year



Global cosmetic hair market 2015 = 81 billions USD

Global cosmetic anti-hair market 2015 = 2 billions USD

Common ingredients:

- Caffeine
- Niacin
- Vitamin B6
- Keratin
- etc

WELL-KNOWN INGREDIENTS

• Vasodilation

Minoxidil (Regain®/Rogain®) an OTC vasodilator medication known for its ability to slow or stop hair loss and promote hair regrowth



5% Minoxidil for men
2% Minoxidil for women

• Hormonal (DHT transformation)

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



• Collagen rigidification & hair anchoring

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





MARKET OPPORTUNITY?

- Minoxidil was first used in medicine for patients suffering from cardio-vascular diseases. The activity on alopecia was later observed as an adverse effect.
- Minoxidil is the n°1 reference in the topical market but:
 - Minoxidil works on 1 person out of 2 & on younger people (18 to 40)
 - Side effects: burning, irritation, redness, chest pain
- Market is looking for alternatives to replace Minoxidil or combine to it in order to:
 - Decrease its concentration and thus side effects
 - Act on complementary targets to improve efficacy

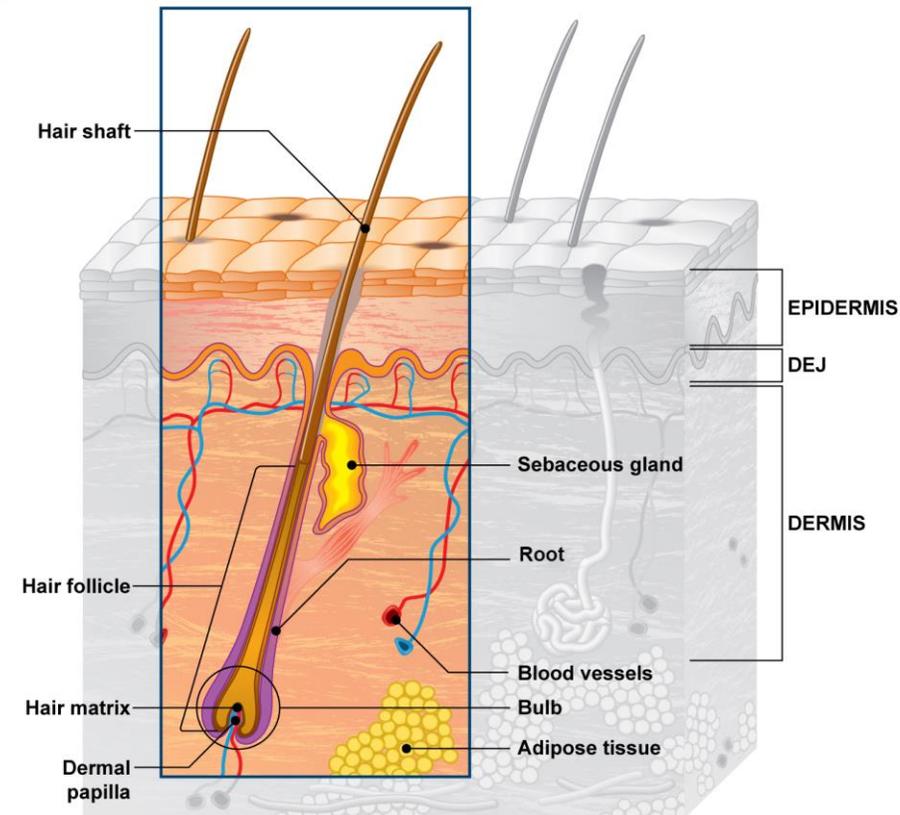
HAIR SCIENCE

Hair structure consists of:

- **Hair shaft:** dead part above skin consisted of an accumulation of keratin (hard protein) produced by the keratinocytes of hair follicle.
- **Hair follicle:** small cavity made up of keratinocytes that extend in dermis. From this organ, an alive root develops as a progressive accumulation of keratinocytes continuously dividing in the hair matrix.

At the base of the follicle is the dermal papilla, a vascular part which brings nutriments and oxygen to grow the attached hair in formation

The hair follicle's healthy condition and size are major criteria for an optimized hair growth.



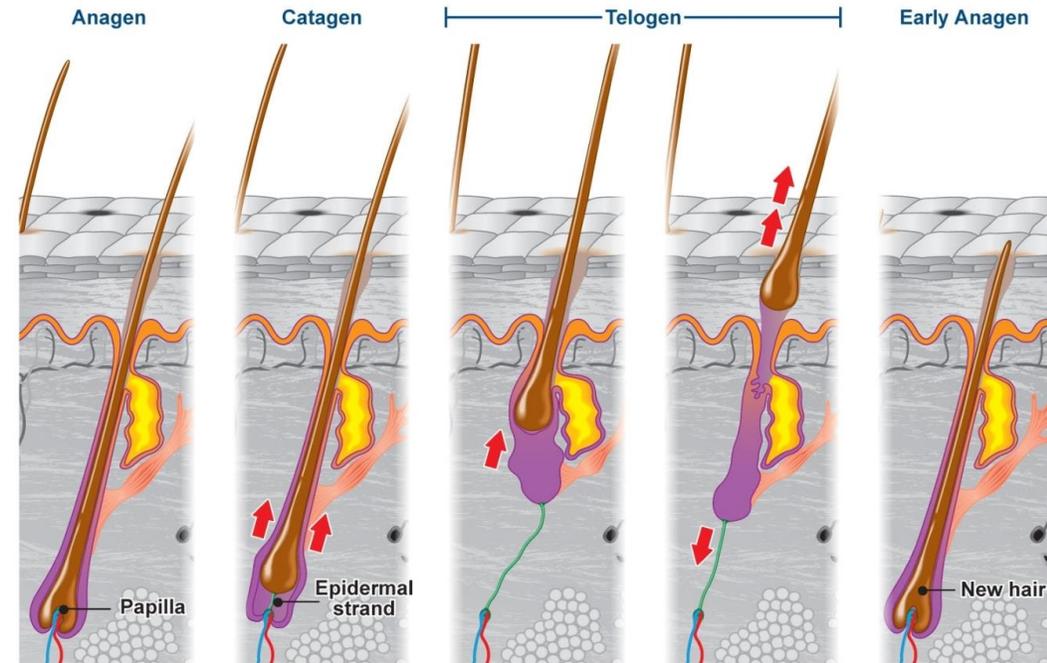
HAIR SCIENCE

Each follicle has the capacity to self-regenerate allowing to grow many hairs over a lifetime (± 20 to 30 hair growth cycles).

The hair follicle / hair growth cycle has 3 distinct phases:

- **Anagen:** (70-85% hair is in **growth phase**). Hair roots grow for 2-6 years due to a progressive and continuous proliferation of keratinocytes in the hair matrix . **Hair follicle is complete (mature) and its activity is optimal.**
- **Catagen:** (1-2% hair is in **regression phase**). The root detaches from the dermal papilla, **the hair follicle shrinks** and migrates toward the scalp and remains in this phase for 2-3 weeks.
- **Telogen:** (15-30% hair is in **resting phase**). Hairs stay attached to the scalp for about 3 months and then fall out. **The degenerated hair follicle starts to regenerate** and migrates downward the bottom of epidermis.

Next hair growth cycle starts when dermal papilla & regenerated follicle join together again & new hair begins to form.



HAIR FOLLICLE : THE KEY PLAYER OF THE HAIR GROWTH CYCLE

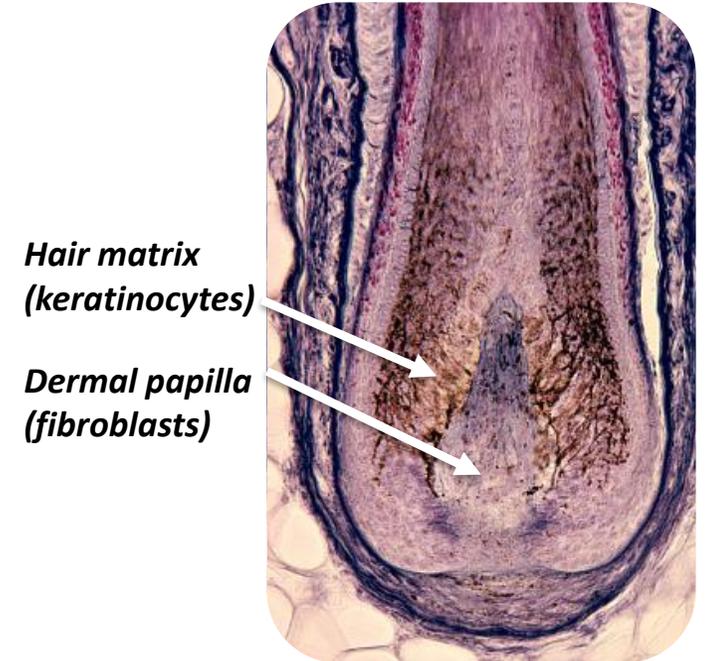
2 key elements control the hair follicle cycle:

DERMAL PAPILLA

- sends signals to rythm cycle phases;
 - its size have a great influence on the quality and size of hair follicle, and then on the quality of the hair in formation;
 - composed of fibroblasts and collagen matrix. Produces anchoring proteins to attach hair.
- => Need to maintain matrix integrity for an optimal size and activity**

HAIR FOLLICLE STEM CELLS (HFSC)

- are responsible to generate, maintain and renew the hair follicle;
 - provide keratinocytes for hair follicle and hair
- => Need to activate HFSC**

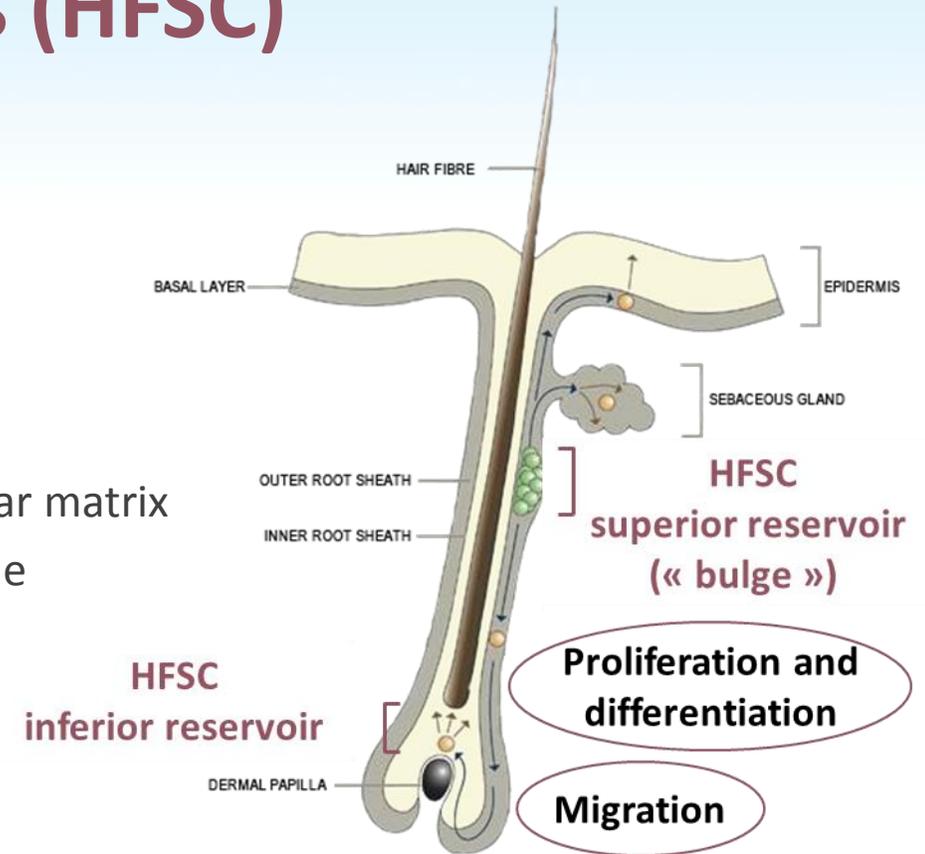


FOCUS ON HAIR FOLLICLE STEM CELLS (HFSC)

- HFSC reside in 2 specific zones:
 - under sebaceous glands (superior reservoir -“bulge”)
 - above the bulb (inferior reservoir)
- HFSC are in a dormant state during telogen phase
 - => Reactivated to regenerate hair follicle during anagen phase
 - => They proliferate (cell division), differentiate into follicular matrix keratinocytes and migrates to the bottom of the hair follicle
 - => Keratinocytes continue to divide and accumulate to form the hair

The activation of HFSC by Capixyl™:

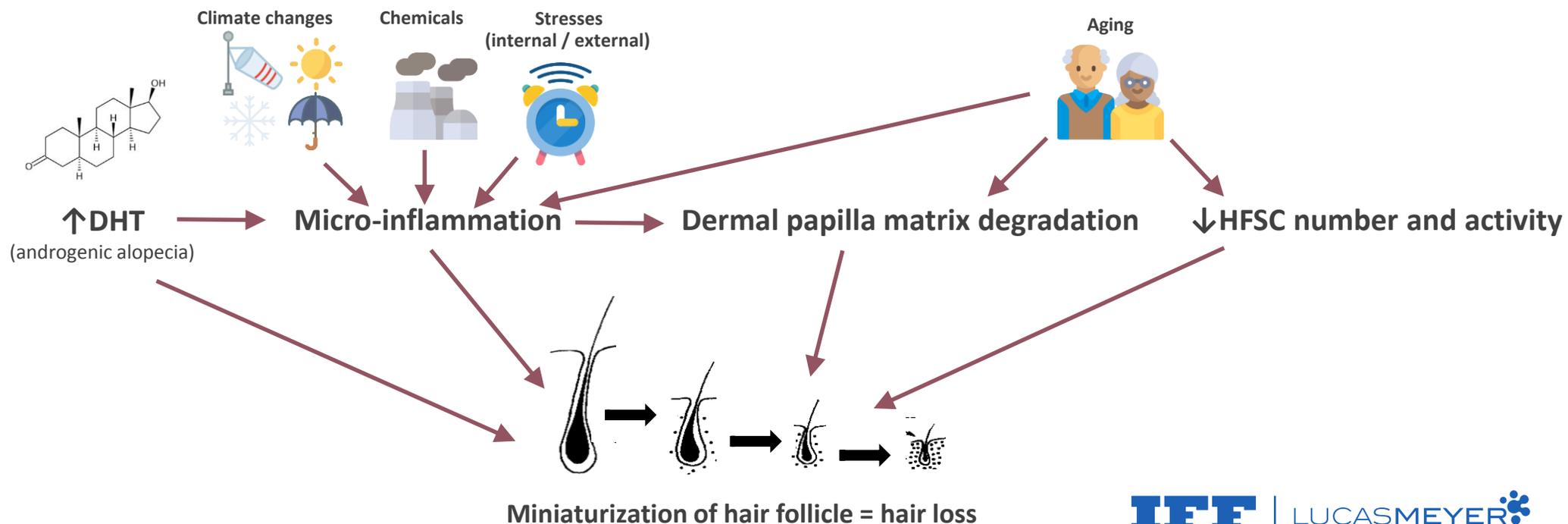
- On existing hair:
 - prolongs growth phase (anagen) of existing hair by maintaining hair follicle => prevention of hair loss
 - improves hair formation by providing higher number of keratinocytes => longer/stronger hair
- On fallen hair:
 - Improves hair regrowth du to a better hair follicle regeneration



HOW IS THE HAIR CYCLE IS DISRUPTED?

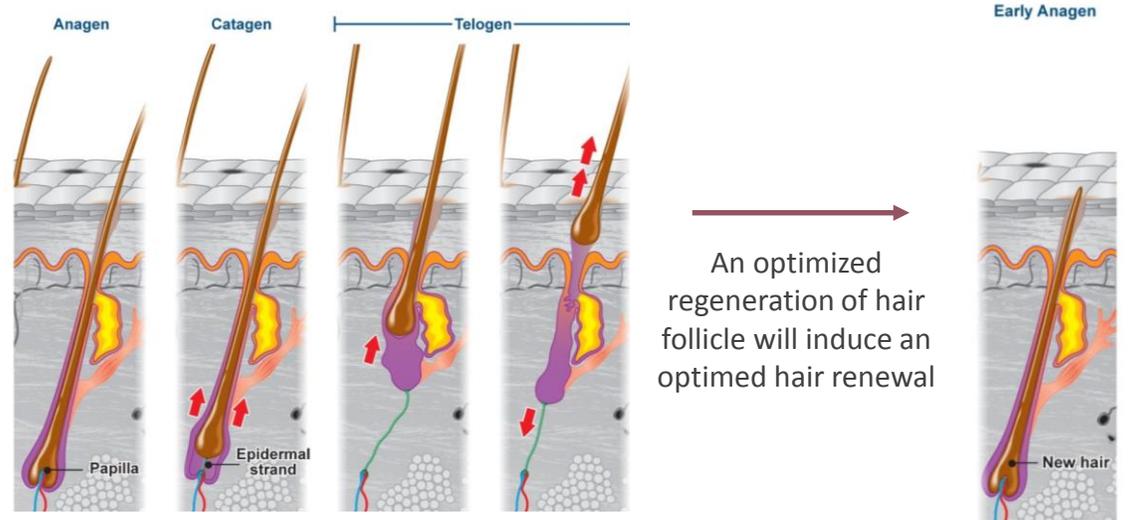
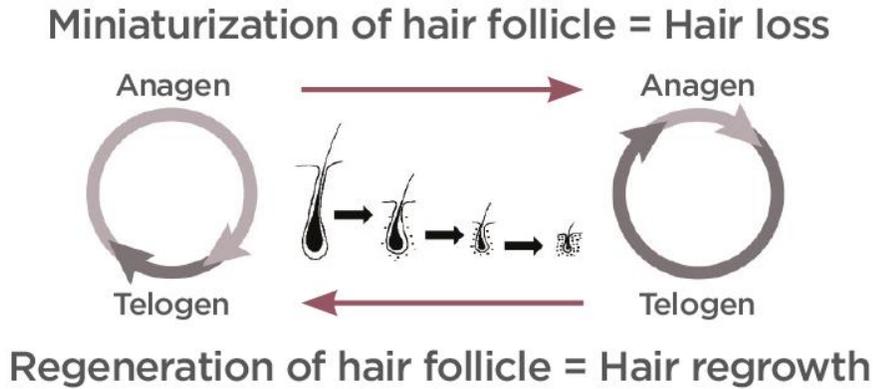
Both **hair thinning and hair loss** are due to a progressive **miniaturization of hair follicle**, associated with a **shorter anagen phase**. Smaller, hair follicle produces thinner hair until it can't produce hair anymore (baldness is the last step).

Several factors are responsible for hair follicle miniaturization (men and women):



HOW TO GROW STRONGER HAIR?

Optimized hair follicle size and health are the key to decrease/prevent hair thinning and loss and to stimulate hair growth.



Maintaining of hair follicle integrity

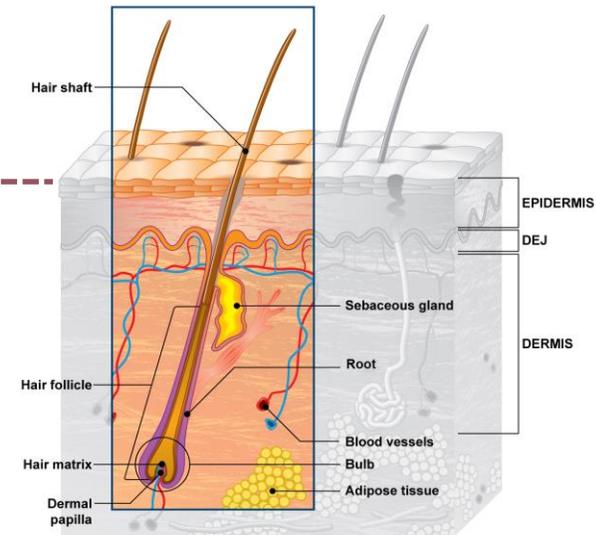
HOW TO GROW STRONGER HAIR?

Healthy and dense grass



- Good soil quality and quantity
- Good nutrition
- Good anchorage

Healthy and dense hair



- Good hair follicle quality and size
- Good nutrition from dermal papilla
- Good anchorage

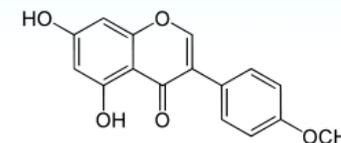
CAPIXYL™: UNIQUE ANTI-HAIR LOSS COMBINATION



Biochanin A extracted from Red Clover (*Trifolium pretense*)

Biochanin A is a powerful flavonoid.

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.



Capixyl™

A clinically proven anti-hair loss active!!!



EX VIVO & IN VITRO TESTS

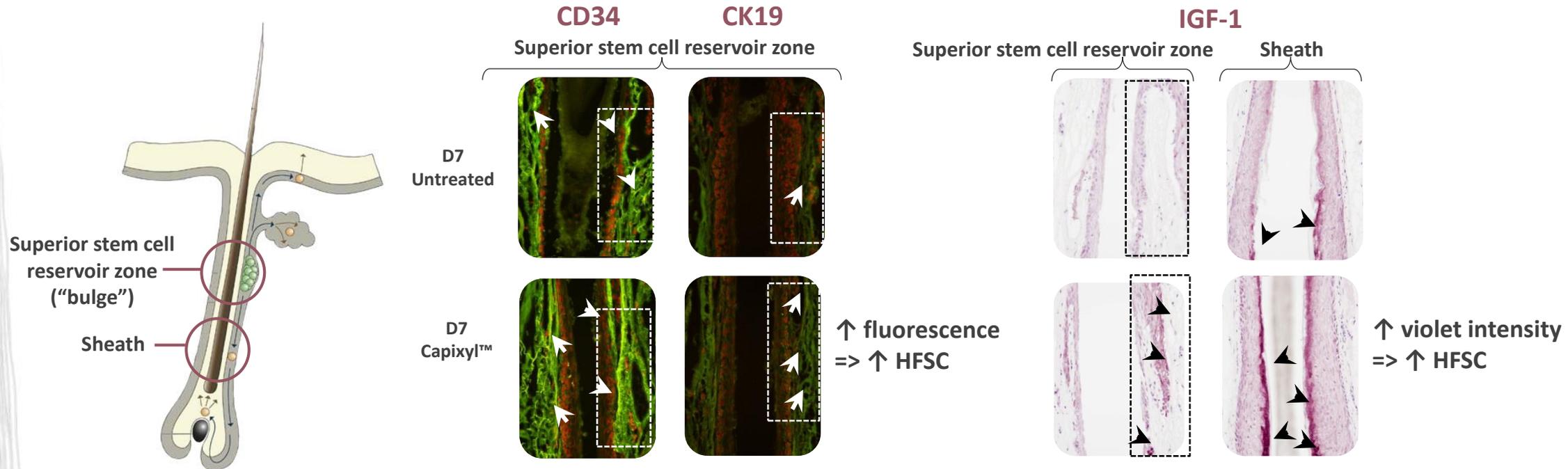
- Effect on hair follicle stem cells
- Effect on hair cell activity
- DHT Modulation (5- α reductase inhibition)
- ECM integrity and anchoring proteins
- Anti-Inflammation effect

STIMULATION OF HFSC ACTIVITY

NEW RESULTS

Ex vivo test protocol

- Hair follicles in anagen phase (from a 49 years old woman) were isolated and treated or not with 1% Capixyl™ during 7 days (Philpott method)
- Staining and cross sections to observe:
CD34, CK19 = specific markers of stem cells (fluorescence) & **IGF-1** = growth factor involved in follicle regeneration (can induce HFSC maturation/differentiation)



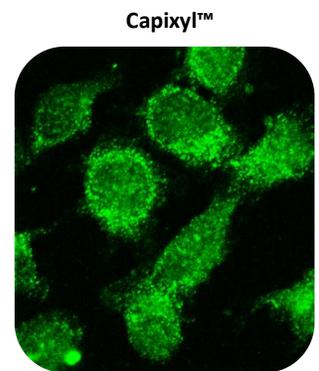
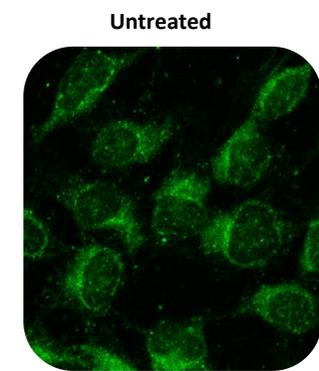
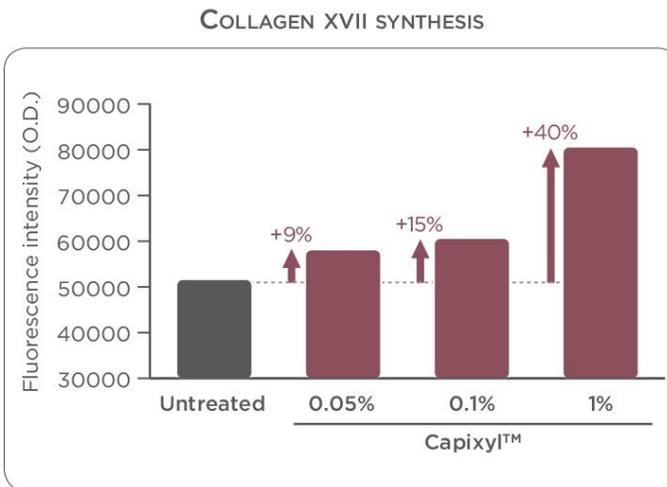
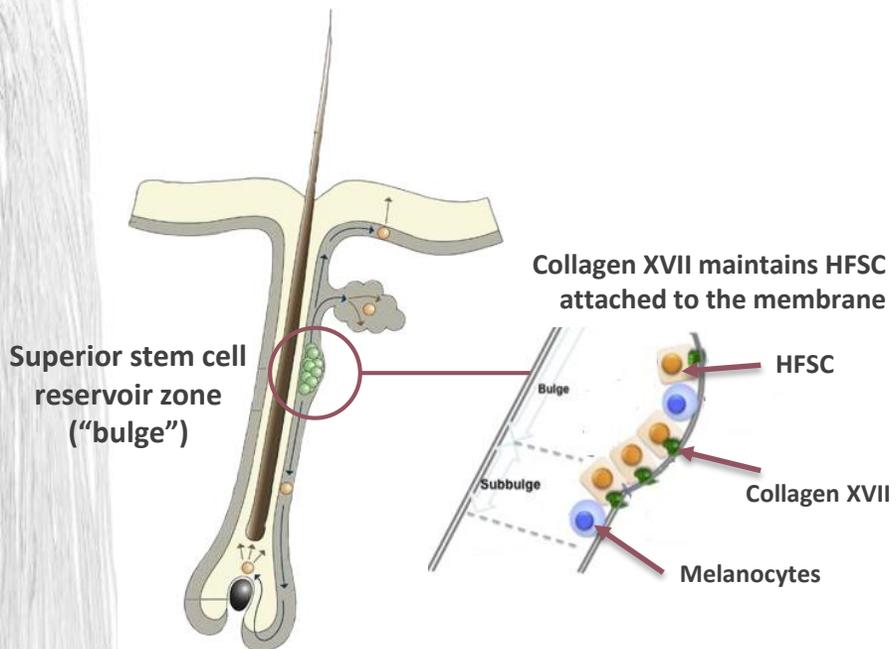
Capixyl™ improves HFSC proliferation and migration for a better hair follicle regeneration

STIMULATION OF COLLAGEN XVII SYNTHESIS



In vitro test protocol

- Keratinocytes treated with Capixyl™ 0.05%, 0.1% and 1% for 24h
- Immunofluorescence labelling of collagen XVII (anchoring proteins)



Capixyl™ stimulates collagen XVII synthesis thus maintaining the high quantity of HFSCs in the reservoir

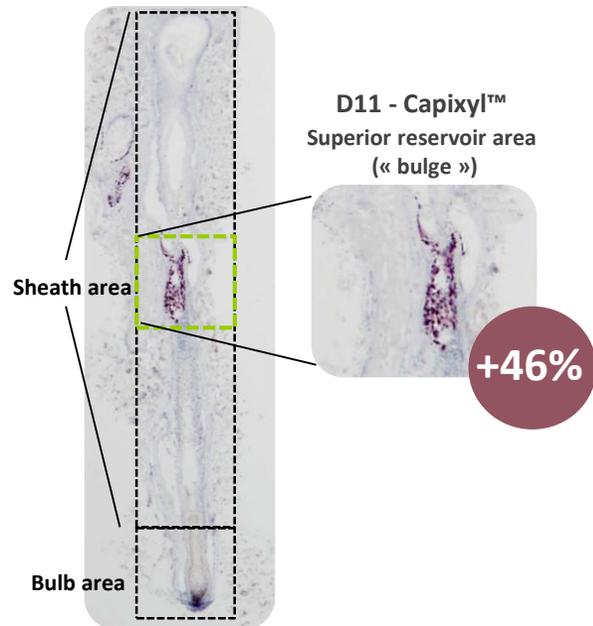
STIMULATION OF CELL ACTIVITY

NEW RESULTS

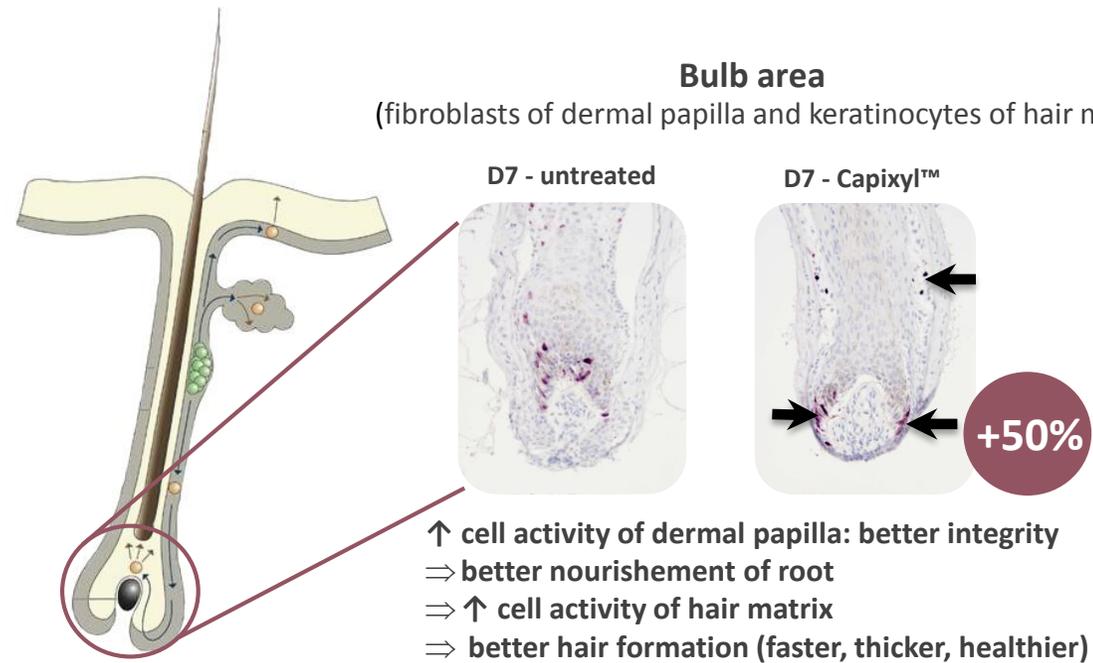
Ex vivo test protocol

- Hair follicles in anagen phase (from a 49 years old woman) were treated or not with 1% Capixyl™ during 11 days (Philpott method)
- Cells in division were identified by immunolabelling of Ki67 (in violet) and quantified in the **bulb** and in the **sheath** areas (including bulge)

Sheath area
(keratinocyte of hair follicle and HFSC in the bulge)



Bulb area
(fibroblasts of dermal papilla and keratinocytes of hair matrix)



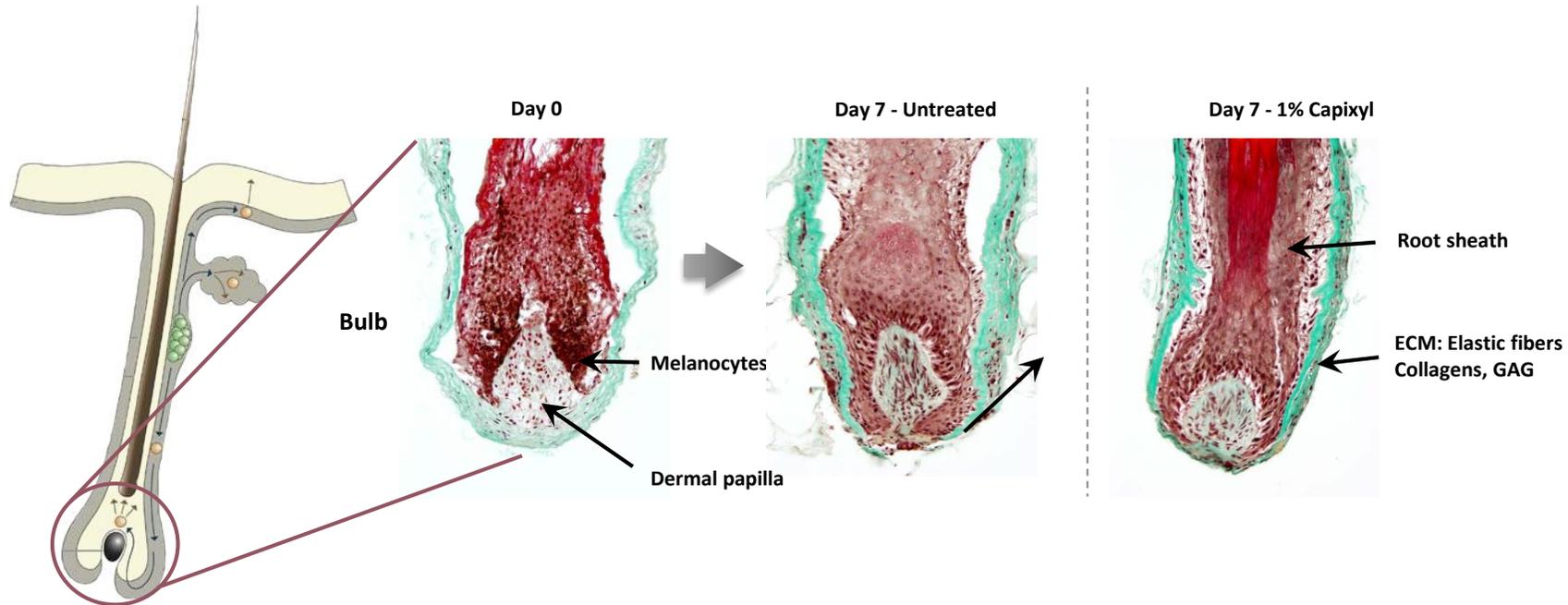
Capixyl™ stimulates cell division favoring optimal hair follicle structure and hair formation

IMPROVEMENT OF HAIR MATRIX MORPHOLOGY



Ex vivo test protocol

- Hair follicles in anagen phase (from a 49 years old woman) were treated or not with 1% Capixyl™ during 7 days (Philpot method)
- Observation of the general morphology by microscopy



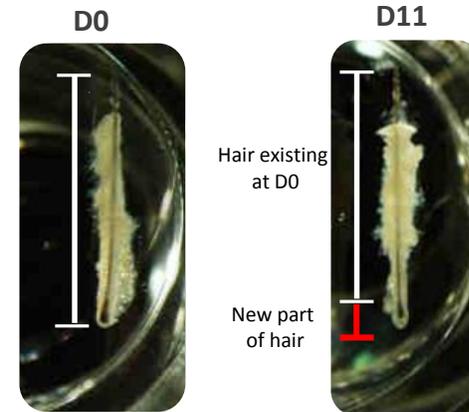
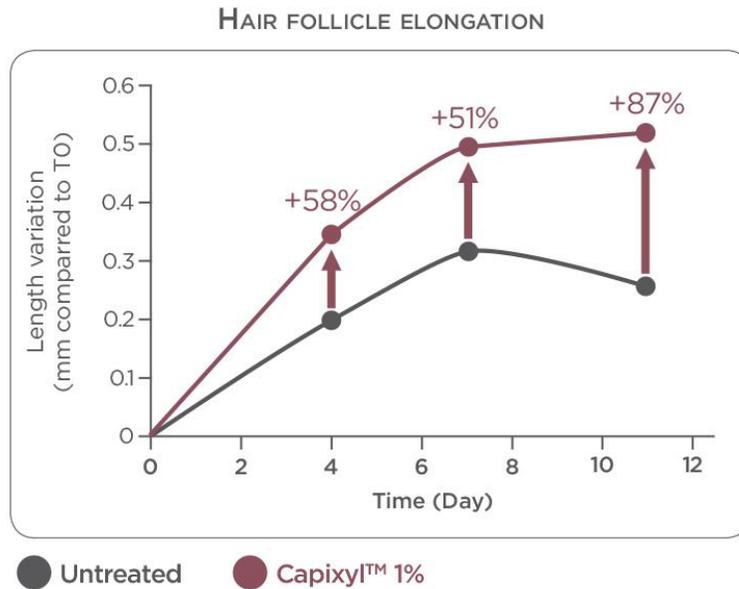
Capixyl™ clearly improves the cohesion of the hair follicle to the ECM, offering optimal environment for higher activity

STIMULATION OF HAIR GROWTH



Ex vivo test protocol

- 2 lots of 17 hair follicles in anagen phase (from a 49 years old woman) treated or not with 1% Capixyl™ during 11 days (Philpot method)
- Hair length variation (=elongation) was measured at D0, D4, D7 and D11 with a micrometer by optical microscope.



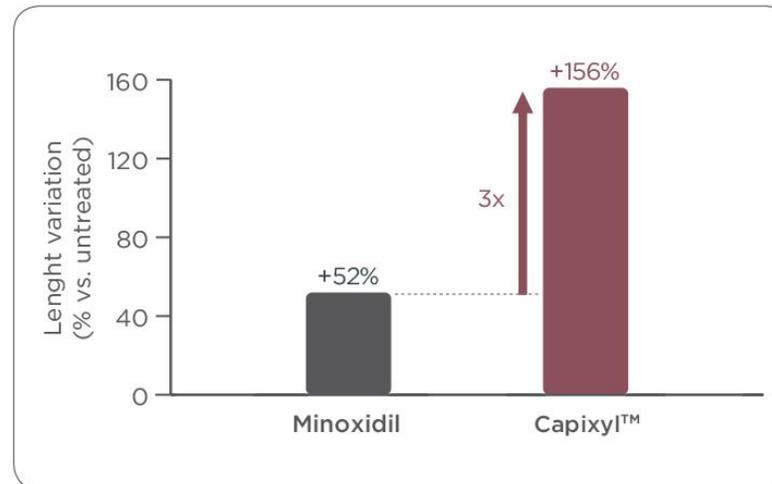
Capixyl™ clearly stimulates hair growth!

STIMULATION OF HAIR GROWTH VS. MARKET REFERENCE

Ex vivo test protocol

- Human hair follicles in anagen phase were cultured with Acetyl Tetrapeptide-3 at 10^{-7} M (\approx 0.016% Capixyl™ solution) or Minoxidil at 120×10^{-7} M during 7 days (Philpot method)
- Hair length variation (=elongation) was measured with a micrometer incorporated in a optical microscope

HAIR FOLLICLE ELONGATION

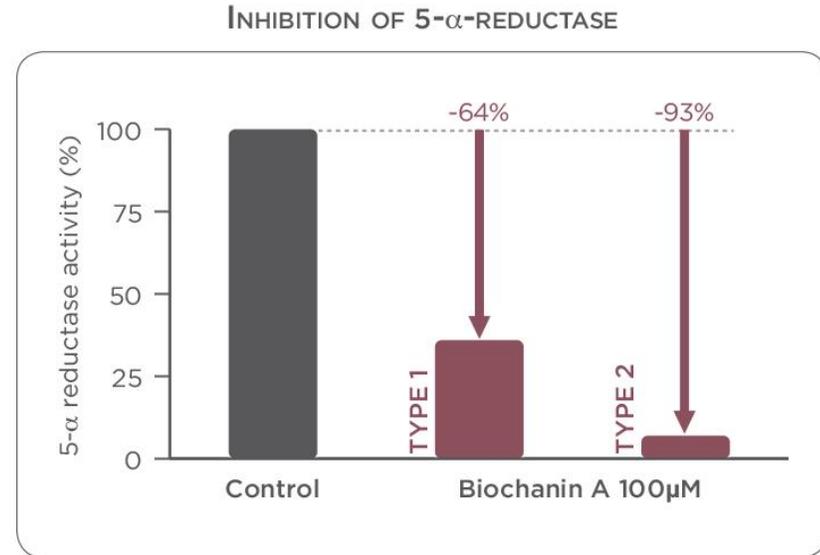


Capixyl™ stimulates hair growth with higher activity than the market reference product, Minoxidil

MODULATION OF DIHYDROTETOSTERONE (DHT)

In vitro test protocol

- Cells were incubated with Biochanin A and radioactive Testosterone
- The amount of labelled DHT and Testosterone was determined by TLC (thin layer chromatography) and scanning.
- Calculation of 5- α reductase activity

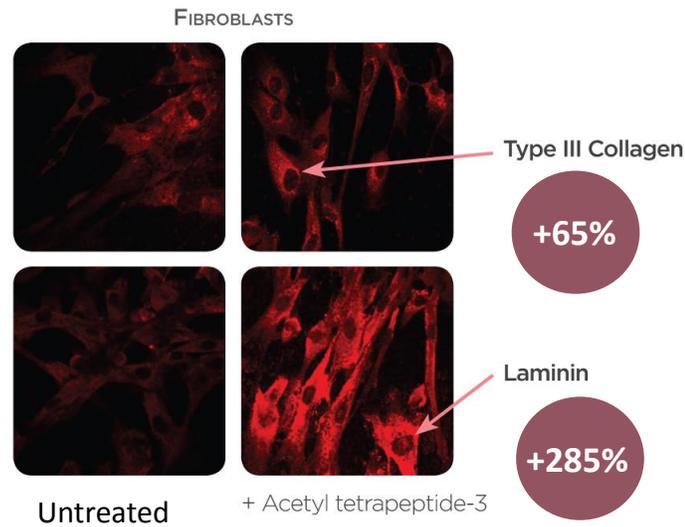


Capixyl™ inhibits 5- α reductase activity, thus confirming the decrease in DHT production to reduce androgenic alopecia

INCREASE IN MATRIX STRUCTURE AND ANCHORING PROTEINS

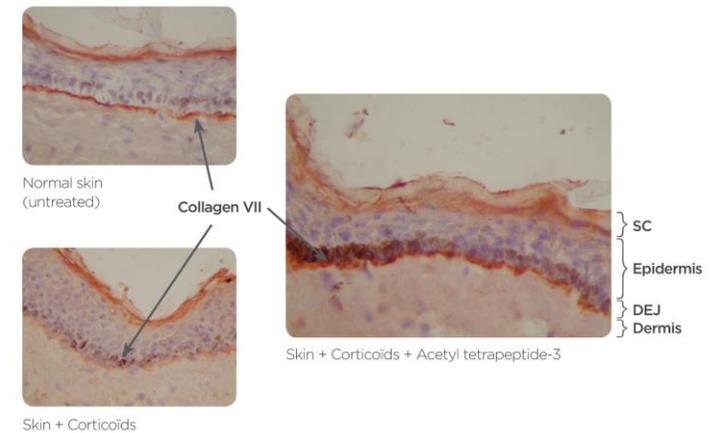
In vitro test protocol (Laminin and Collagen III)

- Human fibroblasts were treated during 3 days acetyl tetrapeptide-3 10^{-7} M
- **Laminin** and **Collagen III** were labelled by immunofluorescence and quantified by image analysis



Ex vivo test protocol (Collagen VII synthesis)

- Human skin explants were pre-treated with dermocorticoids in order to reproduce natural aging pattern.
- Skin explants were then treated with 10^{-3} M Acetyl tetrapeptide-3 during 2 days
- **Collagen VII** was stained and quantified by image analysis



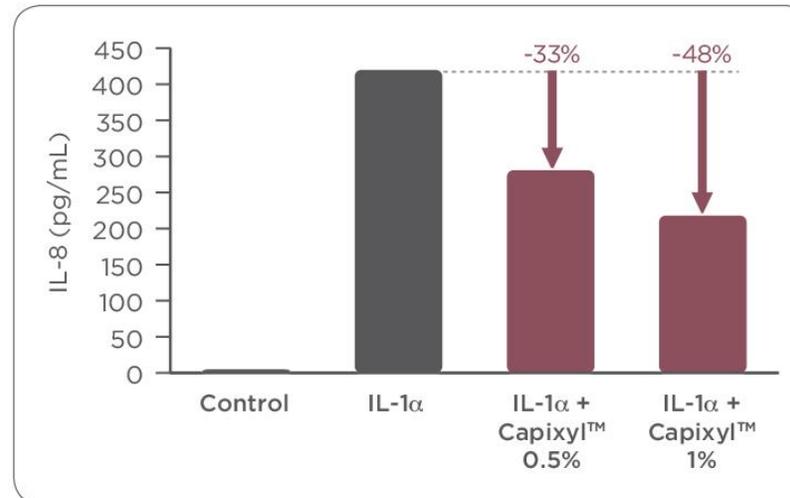
Capixyl™ improves collagens and laminin synthesis favoring dermal papilla structure and hair anchoring

DECREASE IN MICRO-INFLAMMATION

In vitro test protocol

- Inflammation was induced in human fibroblasts with IL-1 α
- Fibroblasts were incubated with Capixyl™ 0.5% and 1% for 24h
- IL-8 quantification using an Enzyme Immunoassay Kit

IL-8 PRODUCTION BY FIBROBLASTS



Capixyl™ decreases pro-inflammatory cytokines production with a dose dependent effect thus limiting hair follicle micro-inflammation

CAPIXYL™ MULTI-TARGET EFFICACY SUMMARY

Activation of Growth

Stimulates the hair follicle regeneration process

NEW RESULTS Preserves Hair Follicle Stem Cell (HFSC) quantity by maintaining them attached to the membrane

NEW RESULTS Activates HFSC by stimulating their proliferation (↑ Ki67, ↑ CD34, ↑ CK19, ↑ IGF-1)

NEW RESULTS Accelerates hair formation by improving bulb cells activity (↑ Ki67)

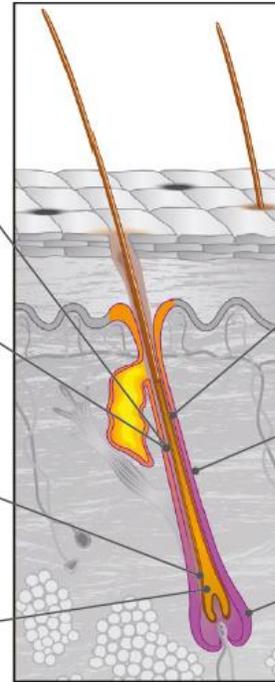
Increases dermal papilla activity by improving its morphology

COLLAGEN XVII
+40%

+46%

+50%

COLLAGEN III
+65%



Limitation of Loss

Reduces the hair follicle miniaturization process

-93% Modulates DHT by inhibiting 5- α reductase activity

IL-8 -48% Reduces local micro-inflammation by decreasing cytokine production

COLLAGEN VII X3 Improves hair anchorage to dermal papilla by increasing anchoring protein production

LAMININ X4



CLINICAL STUDY ON HAIR LOSS



TRICHOGRAM METHODOLOGY

1. Hair **shaving** (~1.8 cm² areas)

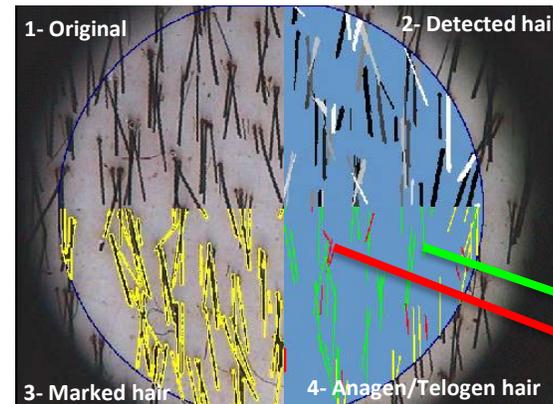
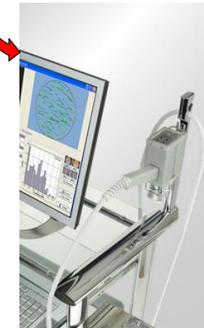


2. **Picture** of the area zones taken with as TricoScan 3 days after shaving to evaluate the number of hair in anagen and telogen phases according their hair growth speed.



Anagen phase was determined as a growth rate of 0.3 mm/day.

3. Image taken by microscopy & automatic digital image analysis

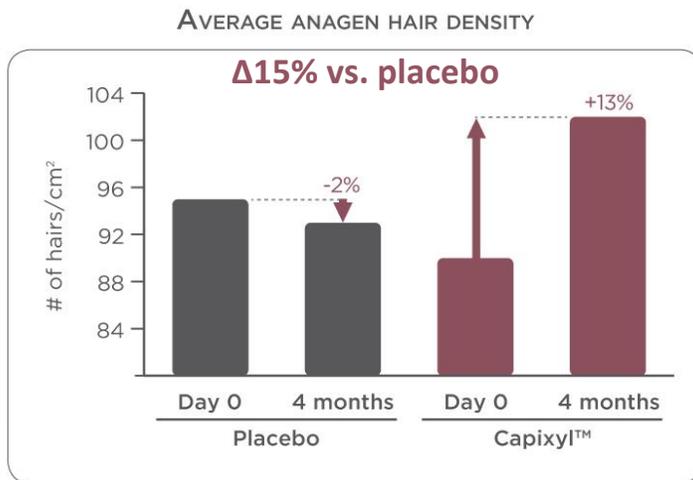


Green : Anagen
Red : Telogen

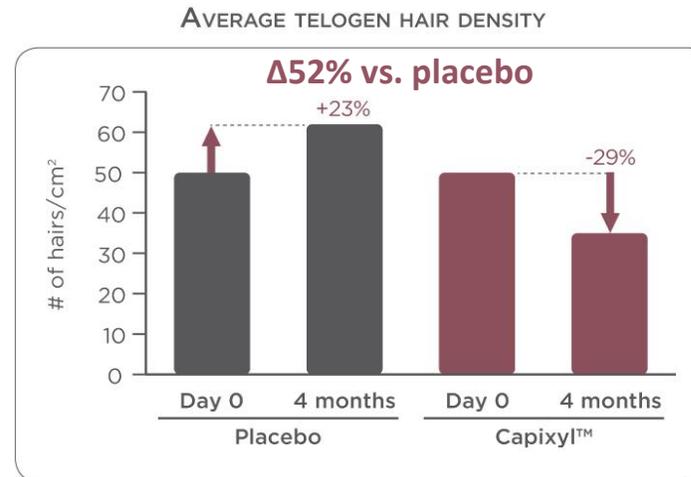
IMPROVEMENT OF HAIR GROWTH CYCLE

In vivo study protocol

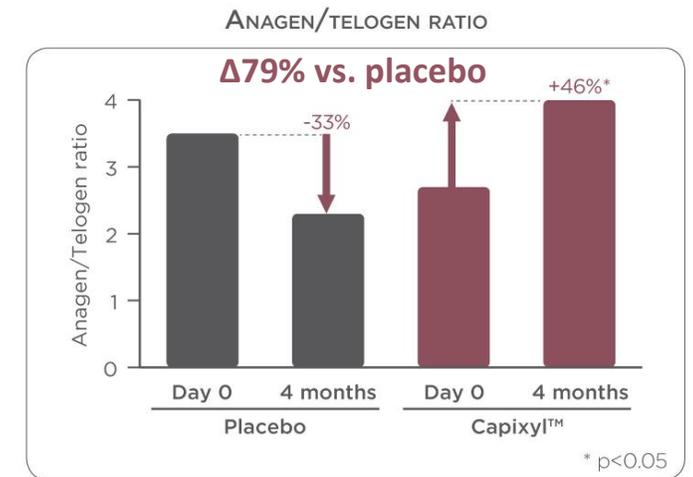
- 30 men with androgenetic alopecia (average age 46) with maximum 200 hair on the treated zone including less than 70% in anagen phase
- 2 groups: 15 treated with a 5% Capixyl™ lotion and 15 treated with a placebo
- 1X/D application at night time of 20 drops of products for a 4 month period
- Quantification of the number of hair per cm² (density) by analysis of digital trichogram (by TrichoScan)



Clear increase in the anagen hair density
= HAIR GROWTH



Strong reduction in the telogen hair density
= STOPS HAIR LOSS



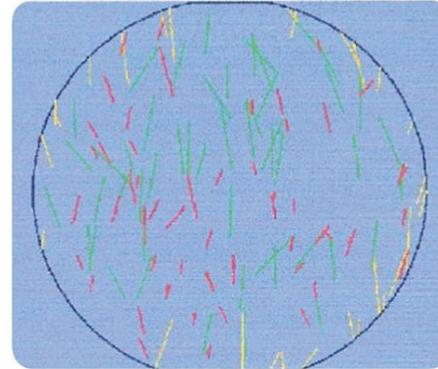
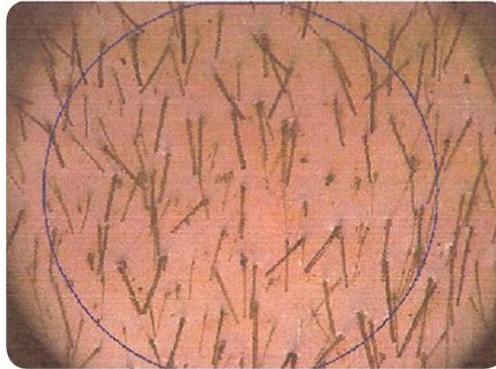
More than 70% of the volunteers saw an
improvement in their condition

**Capixyl™ improves the hair growth cycle and reverses alopecia conditions
with outstanding results!**

Tested formulas: Capixyl 5%, Water 75%, Alcohol 20% - Placebo: Water 75%, Alcohol 20%

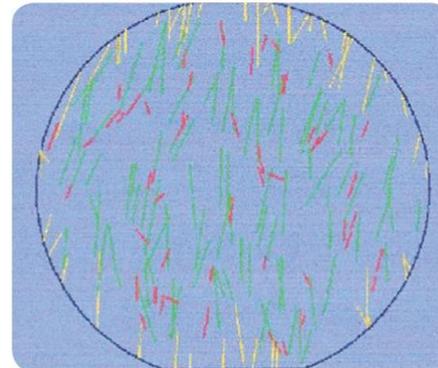
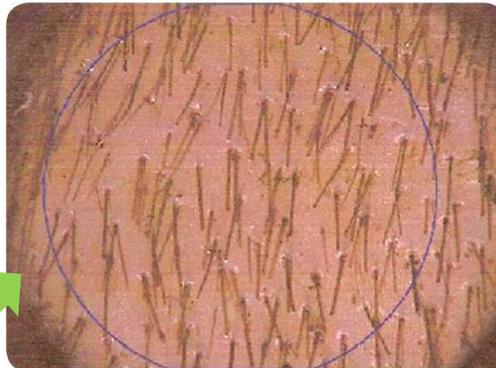
IMPROVEMENT OF HAIR DENSITY

Before
treatment



Green: anagen
Red: telogen

After
treatment



↑ anagen hair
↓ telogen hair

Clear increase in
number of hair!



Capixyl™ is an efficient solution to visibly decrease alopecia



CAPIXYL™ EFFECT ON EYELASHES



HAIR AND LASH SIMILARITIES

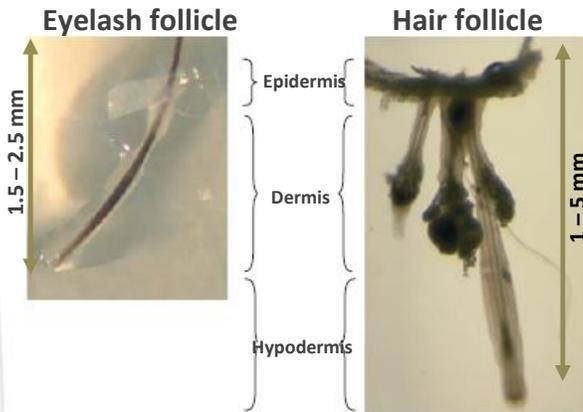
Upper lid: 100-200 lashes; length: 8-12 mm

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

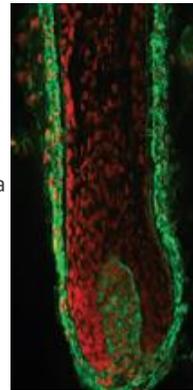


After 40 years old, the number of eyelashes decreases and they become thinner

Eyelash follicle 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



Hair Growth Cycle: Hair vs. Eyelash

	Anagen Growth phase	Catagen Regression phase	Telogen Resting phase	Growth rate
Hair	2 - 6 years 70 - 85% hair	100 days 15 - 30% hair		0.3 - 0.6 mm daily
Eyelash	1 - 3 m (ref.1) 22 - 55 d (ref.2) 15 - 40%	4 - 9 m (ref.1) ~2 m (ref.2) 60 - 85% lashes		0.12 mm daily



ref.1: Ethnic characteristics of eyelashes. Br J. Dermatol. 2006. Na et al. Amorepacific
ref 2: Human eyelashes characteriz ation. Br J. Dermatol. 2010. Thibaut et al. L'OREAL

METHOD

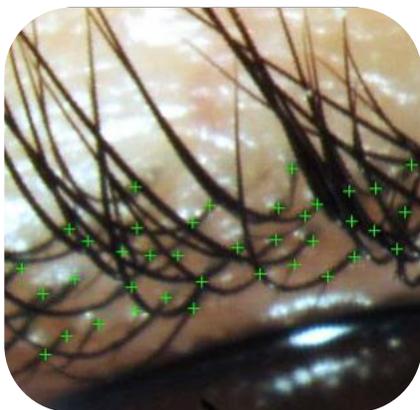
1 - At D0, 4 weeks and 8 weeks, photographs of the upper lashes were taken with a camera fixed on a biomicroscope



Lash density

(number of roots per unit of surface)

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



3 - Measurement of the surface where the lashes growth



Number of young lashes

2bis - Counting the number of new lashes according the morphology and characteristics of young lashes (in comparison with adult lashes):

- less coloring
- thinner
- shorter

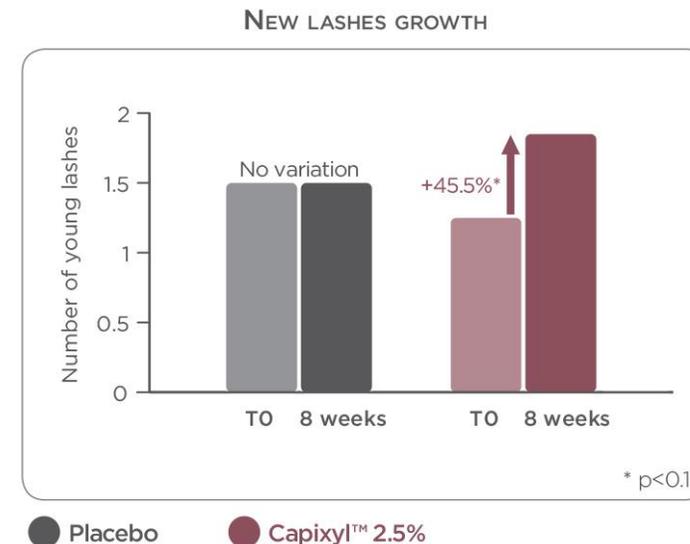
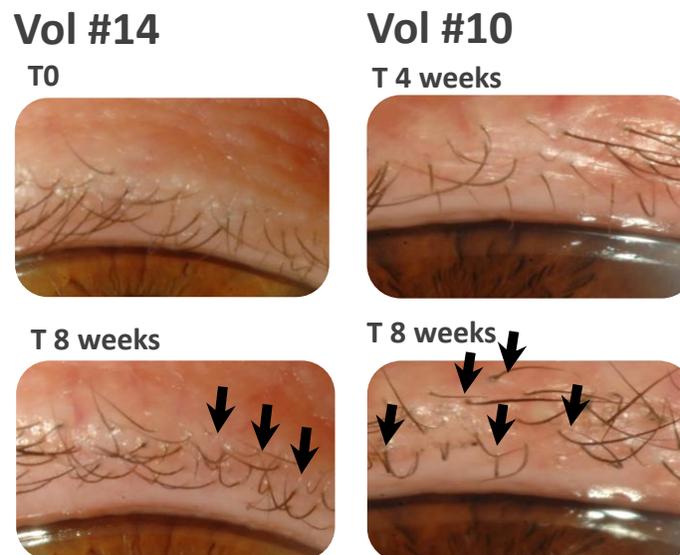
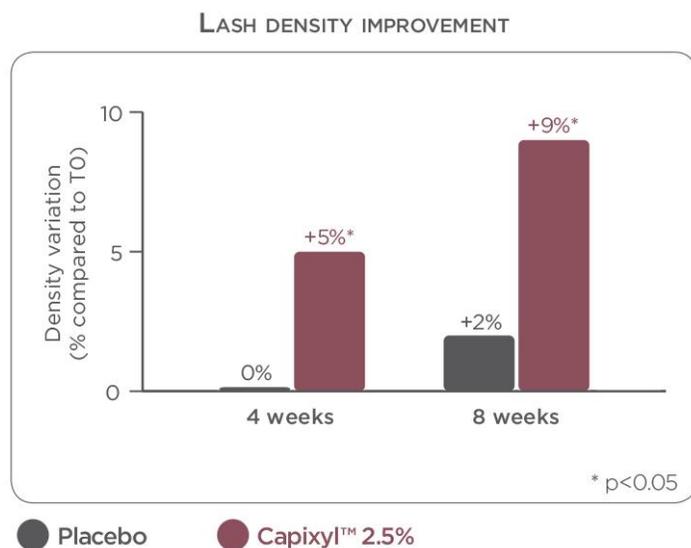


4 - Determination of the lash density

EVALUATION OF THE LASH DENSITY

In vivo study protocol

- 17 women (25-68 years old)
- Application of a 2.5% Capixyl™ gel or a placebo gel on the upper and lower lashes of the eye in the morning and in the evening during 8 weeks
- Evaluation of lash density and number of new lashes at 4 weeks and 8 weeks on image taken with a biomicroscope



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

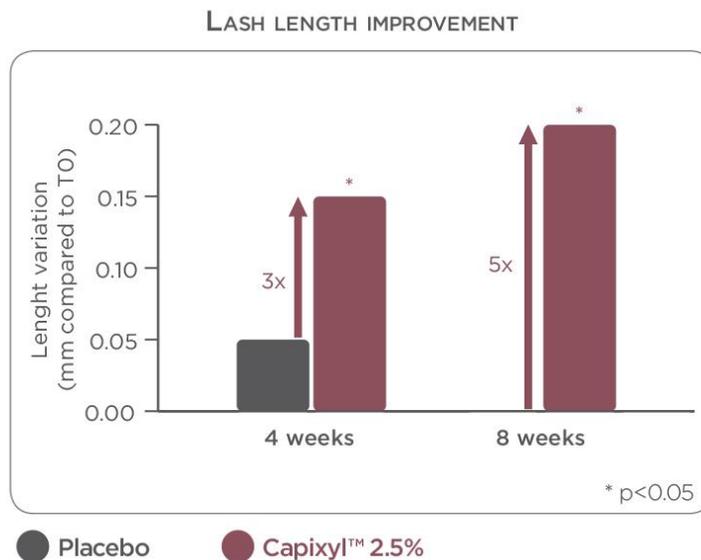
**Capixyl™ induces a clear and significant increase in the lash density
(increase in new lashes & decrease in falling lashes)**

Tested formula: Capixyl™ 2.5%, Water 88.1%, Glycerin 3%, VP/VA Copolymer 2%, Carbomer 1%, Preservatives, Ph adjuster

EVALUATION OF THE LASH LENGTH

In vivo study protocol

- 17 women (25-68 years old)
- Application of a 2.5% Capixyl™ gel or a placebo gel on the upper and lower lashes of the eye in the morning and in the evening during 8 weeks
- Assessment of the mean length of the upper ciliary fringe (for each eye) on photography taken with a digital camera at D0, 4 weeks and 8 weeks



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

Up to 0.70 mm
after 4 weeks!

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

**Capixyl™ significantly improves lash growth
after only 4 weeks**

EVALUATION OF THE LASH LENGTH

Vol #3

T0



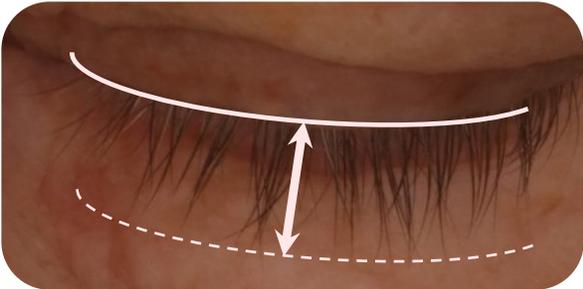
T 4 weeks



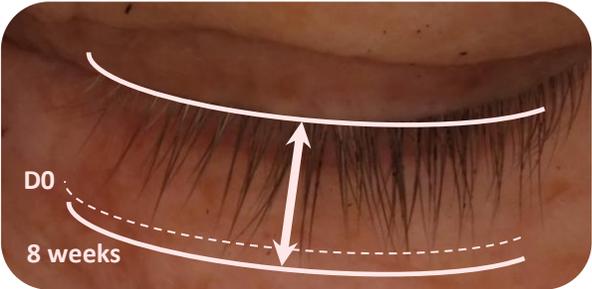
Up to 0.70 mm
after 4 weeks!

Vol #2

T0



T 8 weeks



Vol #16

T0



T 4 weeks



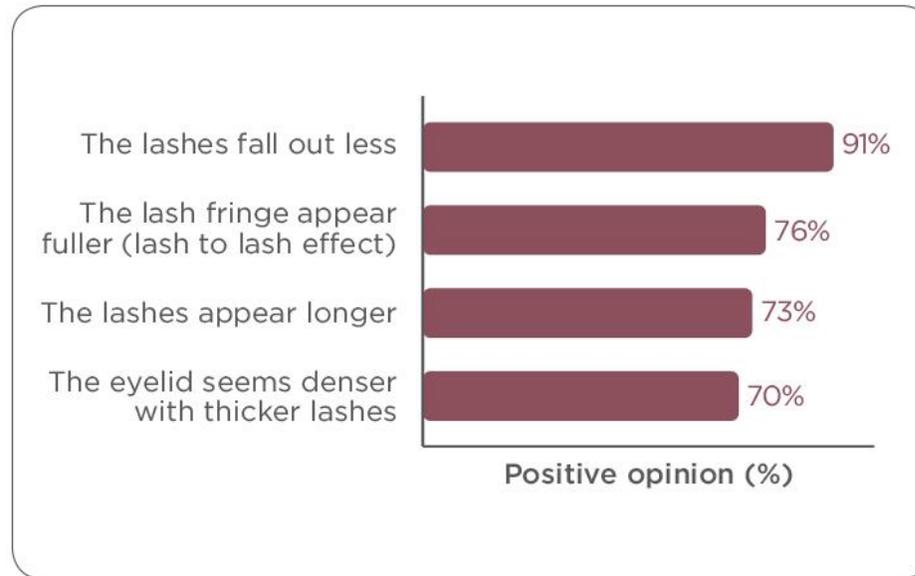
T 8 weeks



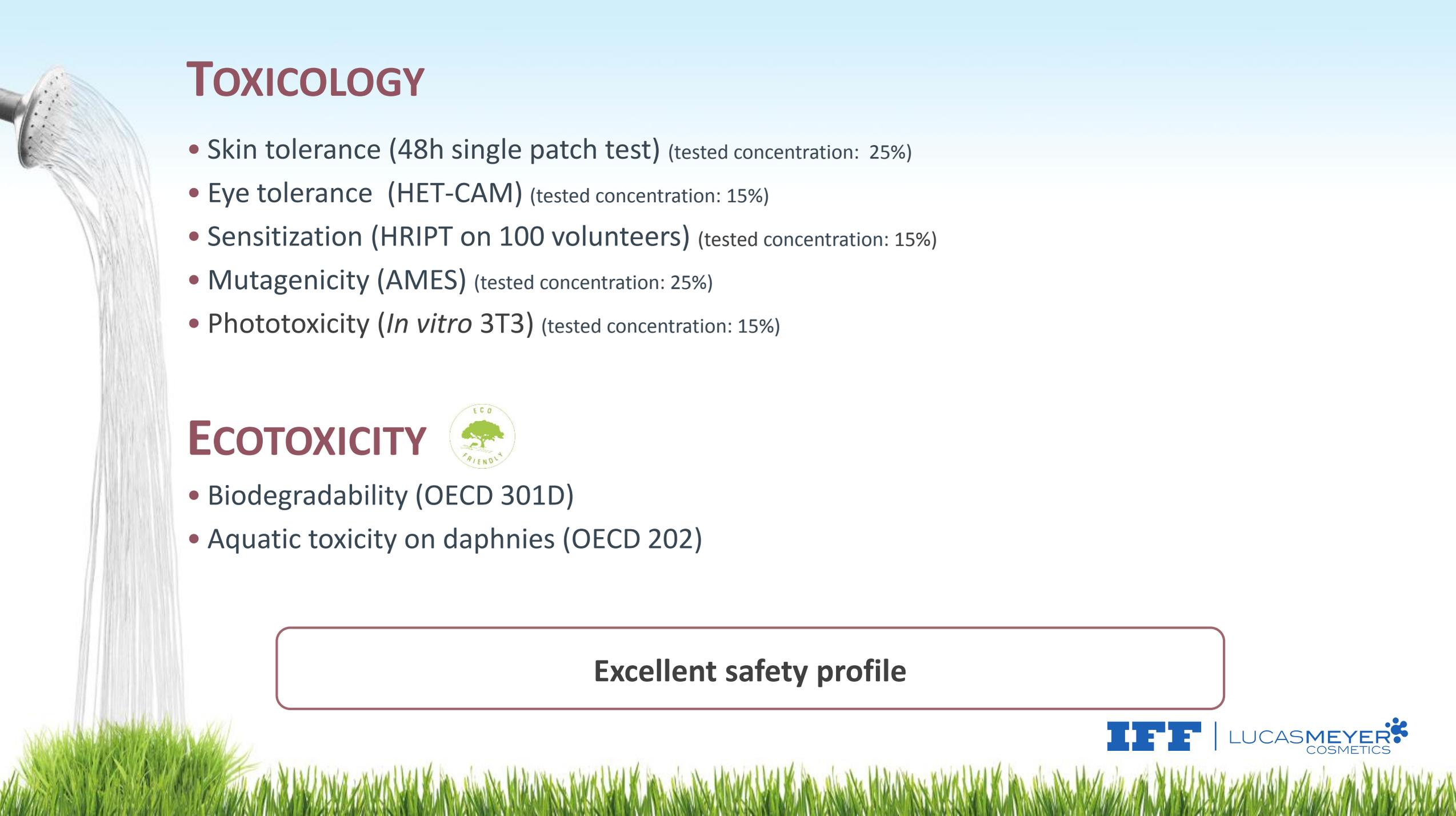
CONSUMER TEST

Protocol

- 17 women (25-68 years old)
- Application of a 2.5% Capixyl™ gel or a placebo gel on the upper and lower lashes of the eye in the morning and in the evening during 8 weeks
- Assessment of the mean length of the upper ciliary fringe (for each eye) on photography taken with a digital camera at D0, 4 weeks and 8 weeks



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



TOXICOLOGY

- Skin tolerance (48h single patch test) (tested concentration: 25%)
- Eye tolerance (HET-CAM) (tested concentration: 15%)
- Sensitization (HRIPT on 100 volunteers) (tested concentration: 15%)
- Mutagenicity (AMES) (tested concentration: 25%)
- Phototoxicity (*In vitro* 3T3) (tested concentration: 15%)

ECOTOXICITY



- Biodegradability (OECD 301D)
- Aquatic toxicity on daphnies (OECD 202)

Excellent safety profile

CAPIXYL™ HAIR FERTILIZER

IMPROVES HAIR GROWTH CYCLE

- Stimulates hair follicle regeneration/decreases hair follicle miniaturization
- Improves growth phase (anagen) and reduces loss phase (telogen)
- Provides faster results than market reference

SYNERGISTIC COMPLEX

- Biomimetic peptide
- Red clover flower extract rich in biochanin A

MULTI-TARGET ACTION

- Preserves hair follicle stem cells (HFSC)
- Modulates DHT (↓ 5-α reductase)
- Stimulates dermal papilla matrix and anchoring proteins synthesis (collagen III, collagen VII and laminin)
- Decreases microinflammation (↓IL-8)



CONSUMER BENEFITS

- Helps provide stronger, thicker, healthier and fuller hair, lashes and eyebrows
- Anti-thinning effect
- Visible results without adverse event

MANUFACTURER BENEFITS

- Efficient cosmetic alternative to Minoxidil
- Complements Minoxidil mechanism of action for more efficient results
- Easy-to-formulate in all types of formulas for hair and eyelashes



CAPIXYL™ PRODUCT INFORMATION

INCI NAME	Water (and) Butylene Glycol (and) Dextran (and) Acetyl tetrapeptide-3 (and) Trifolium Pratense (Clover) Flower Extract	
ADDITIVE	None	
APPEARANCE	Transparent liquid	
FORMULATION	Should be incorporated at the end of the formulation at a temperature below 40°C	
DOSAGE	0.5-2.5%: preventive care	2.5-5 %: intensive treatment
OPTIMUM PH	4.0 - 8.0	
APPLICATIONS	HAIR (leave on & rinse off) <ul style="list-style-type: none">•Anti-hair loss products•Hair regrowth products•Anti-aging hair care products•Hair treatment for menopausal women•Treatment for seasonal hair loss	EYELASH/EYEBROW <ul style="list-style-type: none">•Serum•Mascara•Pencil•Make up remover



PRESERVATIVE FREE

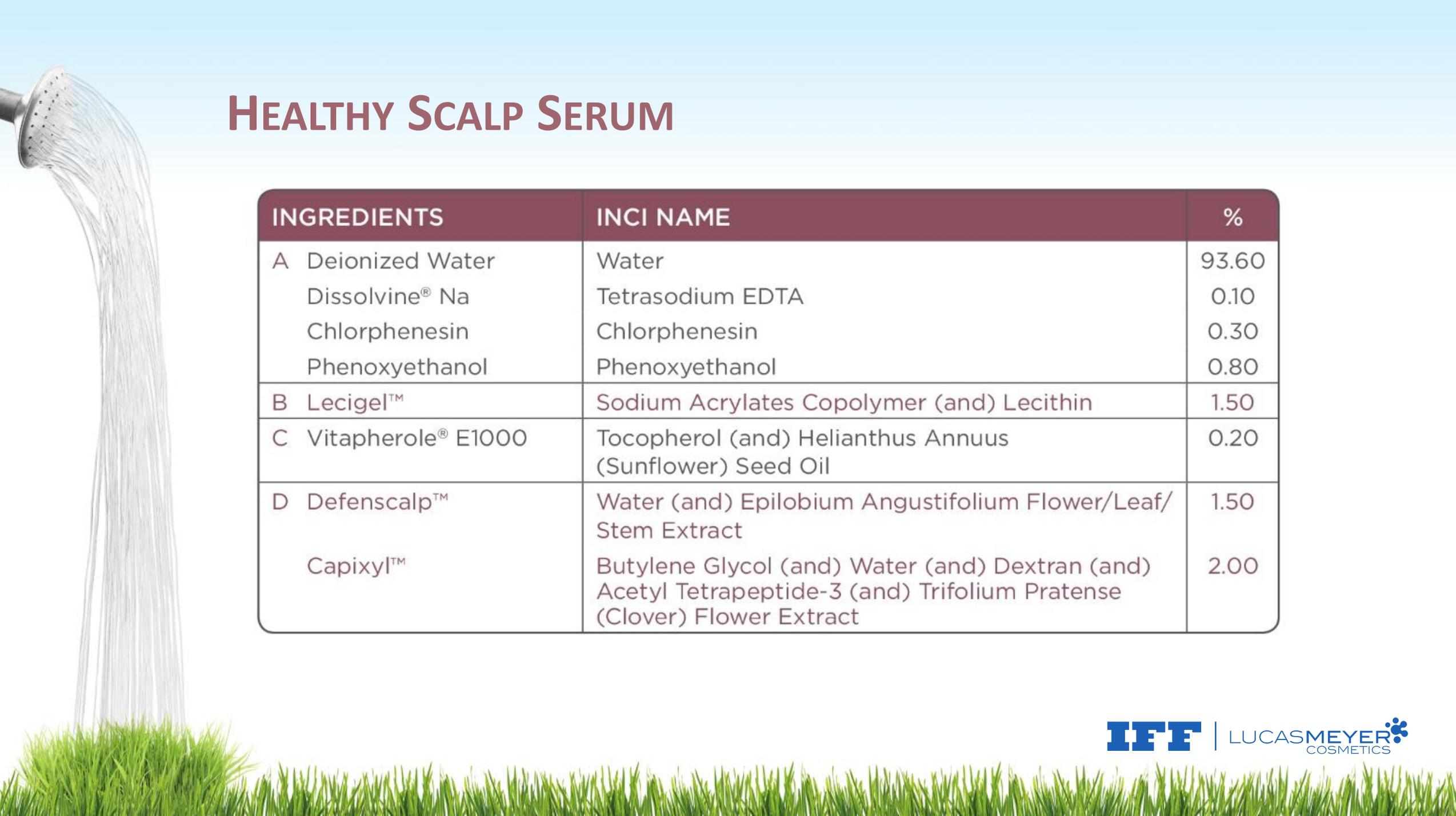


CHINA COMPLIANT



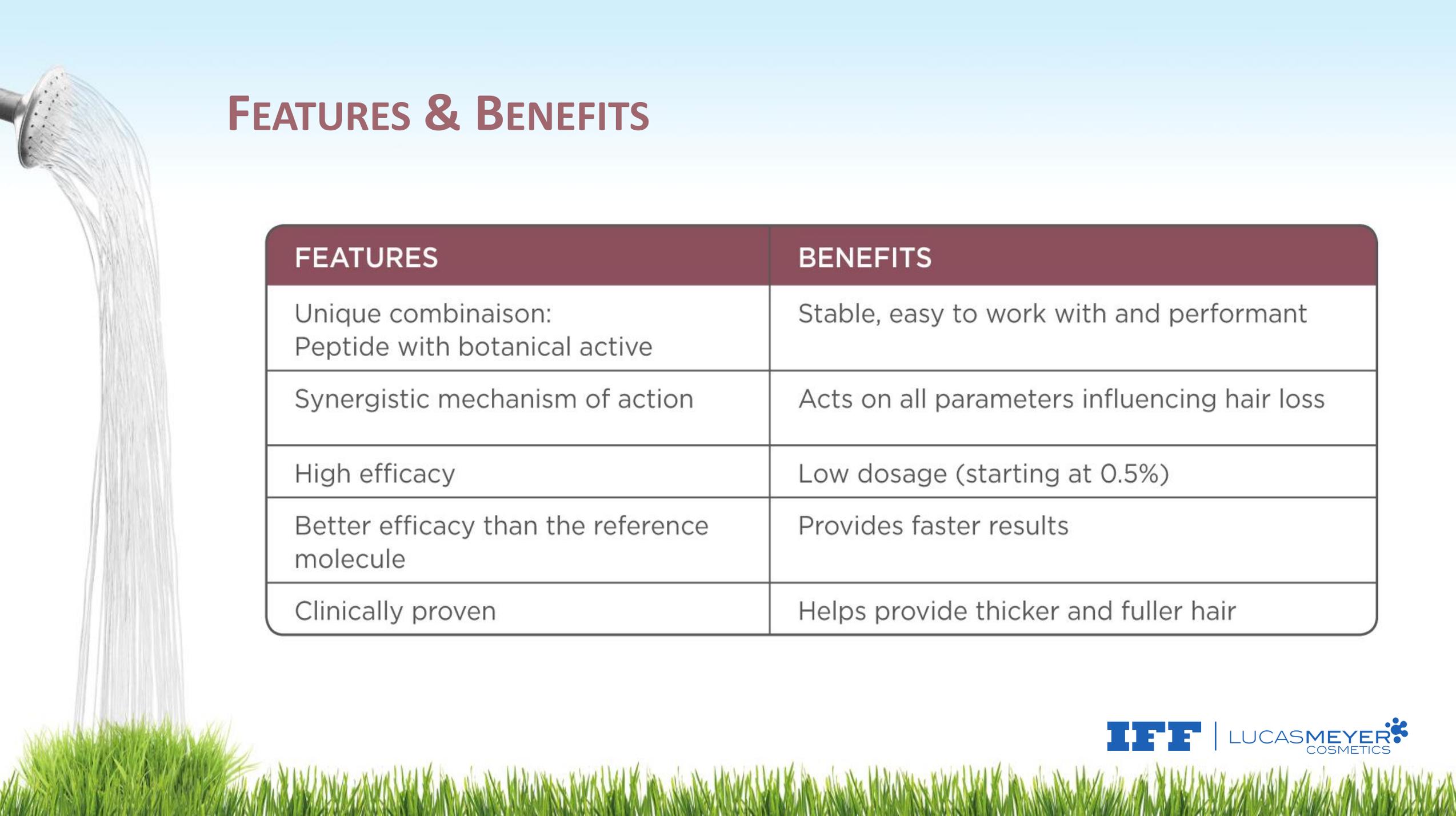
ECOFRIENDLY





HEALTHY SCALP SERUM

INGREDIENTS	INCI NAME	%
A Deionized Water	Water	93.60
Dissolvine® Na	Tetrasodium EDTA	0.10
Chlorphenesin	Chlorphenesin	0.30
Phenoxyethanol	Phenoxyethanol	0.80
B Lecigel™	Sodium Acrylates Copolymer (and) Lecithin	1.50
C Vitapherole® E1000	Tocopherol (and) Helianthus Annuus (Sunflower) Seed Oil	0.20
D Defenscalp™	Water (and) Epilobium Angustifolium Flower/Leaf/Stem Extract	1.50
Capixyl™	Butylene Glycol (and) Water (and) Dextran (and) Acetyl Tetrapeptide-3 (and) Trifolium Pratense (Clover) Flower Extract	2.00



FEATURES & BENEFITS

FEATURES	BENEFITS
Unique combinaison: Peptide with botanical active	Stable, easy to work with and performant
Synergistic mechanism of action	Acts on all parameters influencing hair loss
High efficacy	Low dosage (starting at 0.5%)
Better efficacy than the reference molecule	Provides faster results
Clinically proven	Helps provide thicker and fuller hair



THANK YOU!