[F-HAIR MEN]

Product identity

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.
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.
F-HAIR MEN is an exclusive products that treats effectively alopecia, it was formulated with a blend of peptides, growth factors, organic silicium, pantenol and hyaluronic acid.

Benefits

- Prevents hair loss.
- Stimulates hair growth.
- Reduces hair oxydation process and hair descoloration.
- Fortifies the hair folicules and the hair strucutre.
- Protects the hair.

Active ingredients

- Hyaluronic acid 0,1%
- D-panthenol 0,2%
- Trifolium pratense (clover) flower extract 1%
- Decarboxy carnosine 1%
- Dimethylsilanediol salicylate 1,4%
- Acetyl tetrapeptide-3
- CG-VEGF growth factor
- CG-aFGF
- CG-Copper peptide
- CG-IDP2

Formulation specificities

- Sterilized by filtration.
- No paraben, alcohol, fragrance, animal origin ingredients, colouring and silicone.
- Non-animal tested.

User indications

- Topical application.
- Skin needling.
- Needle-free mesotherapy.
- Iontophoresis.
- Electroporation.
- Meso.

Meso protocol:

Depth: 1 to 2 mm.
Quantity per point: 0.03 to 0.05 cc.
Technique: Nappage.
Needle: 30 G.

Can be mixed with:

Use the product pure.

[Acetyl tetrapeptide-3 + biochanin A complex]

Name: Acetyl tetrapeptide-3, Trifolium Pratense (clover) Flower Extract
Effect: Hair regrowth and alternative to minoxidyl
Reduces the inflammation process by reducing IL-8, stops hair loss and stimulates the hair growth (comparative study to minoxidil) modulates DHT by 5-a reductase inhibition, stimulates the extra cellular matrix and anchoring proteins.
Source:
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 is a 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.
Vectorisation: dextran
Dosis in F-HAIR MEN: 2.5%

About hair loss
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.

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

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

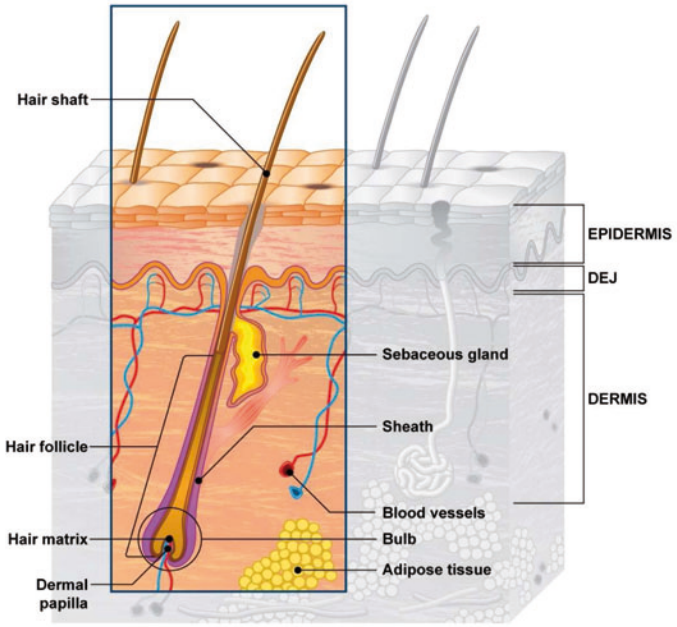
Collagen rigidification & hair anchoring
Aminexil® a patented molecule by L'Oréal fights against the stiffening of hair roots, and thus preserves the tissue surrounding the hair bulb.

[Acetyl tetrapeptide-3 + biochanin A complex]

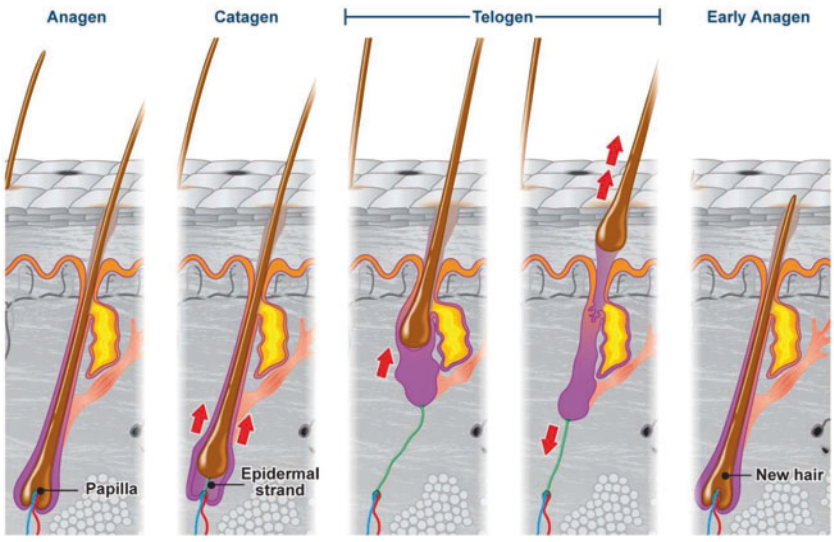
Hair science

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.



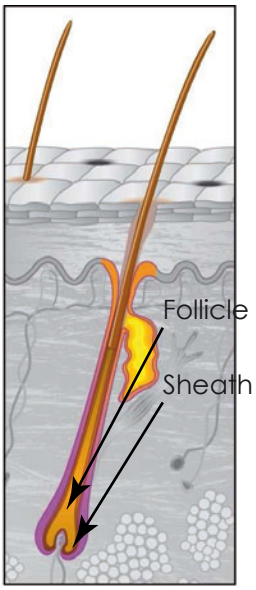
We carries ±100 000 hair follicles. Each follicle can grow many hairs over a lifetime (±20 times). The hair follicle growth cycle has 3 distinct phases:
- Anagen: (Growth phase 70 – 85% hair). Hair are growing for 2- 6 years.
- Catagen: (Transition phase – 1-2%). The hair bulb separates from the dermal 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).



[Acetyl tetrapeptide-3 + biochanin A complex]

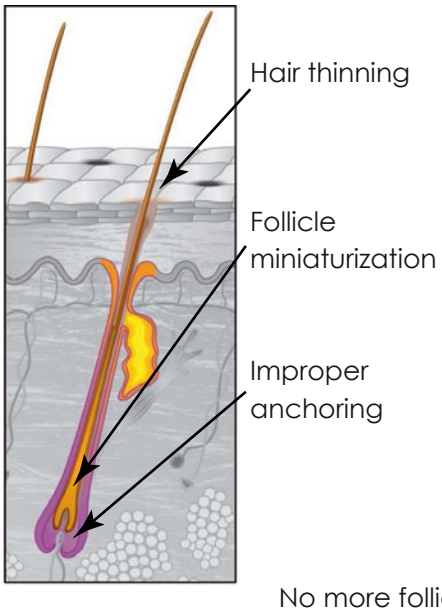
Hair Loss: How it works?

Normal hair growth cycle



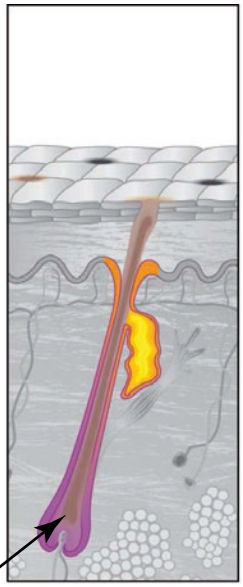
- **No hormonal dysfunction**
- **ECM proteins integrity**
- **No inflammation**

Altered hair growth cycle
(less Anagen + more Telogen)



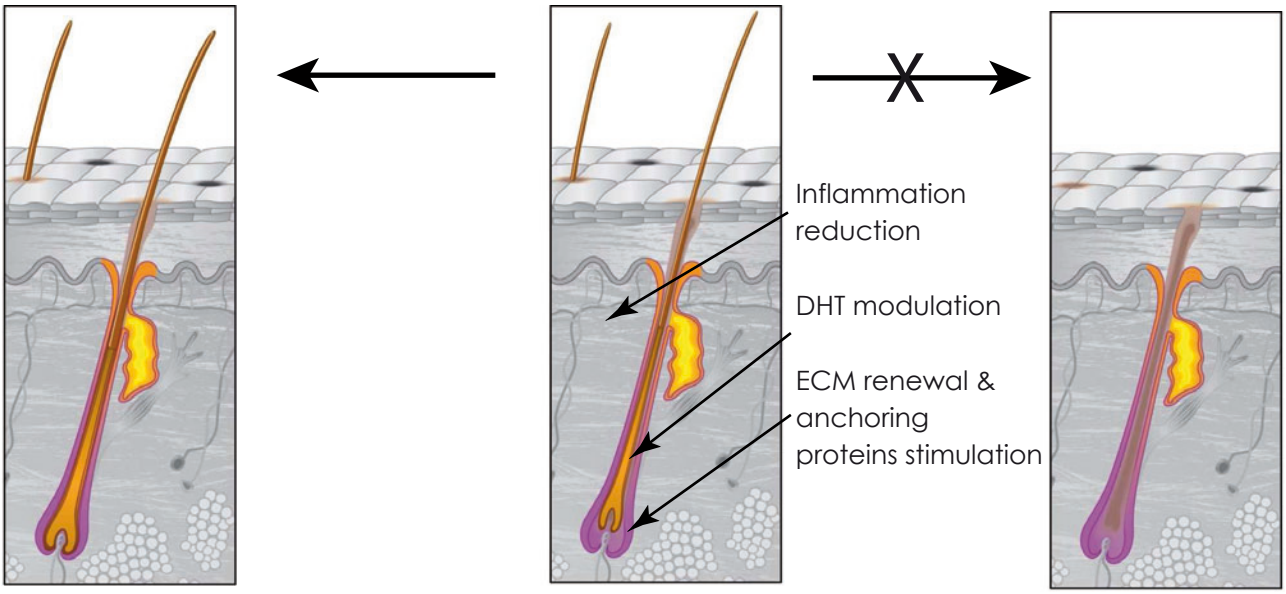
- **DHT increases: shorthens Anagen phase > Miniaturization of follicles**
- **Loss of ECM proteins renewal > Follicle size reduction & loss of hair anchoring**
- **Inflammation > Disruption of hair cycle**

Hair loss



Action mechanism of acetyl tetrapeptide-3 + biochanin A complex in details:

- **DHT Modulation**
- **ECM Integrity**
- **Inflammation**



[Acetyl tetrapeptide-3 + biochanin A complex]

Effect of dihydrotestosterone (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.

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.

Effect of Inflammation

The production of pro-inflammatory cytokines produces an alteration of the ECM and then the hair follicle degradatio followed by hair loss.

Clinical efficacy on Hair Loss

In vivo 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 a lotion containing 5% of complex 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 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

More than 70% of the volunteers saw an improvement in their condition.
The average Anagen (Growth) hair density was improved of 15% vs placebo
The average Telogen (Fall) hair density was decreased of 51% vs placebo

Conclusions: the product induces a clear increase in the anagen hair density = HAIR GROWTH and induces a strong reduction in the telogen hair density = STOPS HAIR LOSS.

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.

The product 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

[Acetyl tetrapeptide-3 + biochanin A complex]

Comparative study with Minoxidil®

Objective

To measure the growth speed of hair shafts on isolated human hair follicles in cultured with Acetyl tetrapeptide-3 in comparison with the Minoxidil®.

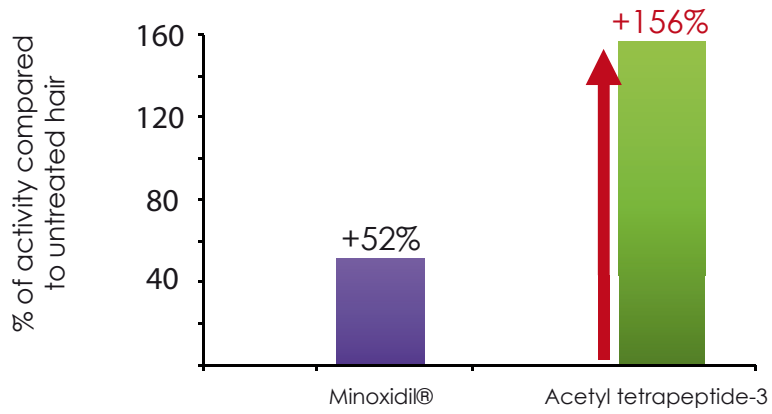
Protocol

• Human hair follicles are recovered from human scalps in anagen phase

• Hair follicles are cultured with Acetyl tetrapeptide-3 at 10-7M (≈ 0.016% CapixylTM solution) or Minoxidil® at 120 X 10-7M for 7 days according to Philpot method

• Evaluation of hair growth after treatment with a micrometer by optical microscope and measurement of the normalized activity after treatment (= hair growth induced by the treatment)

Hair growth activity of the treatment compared to untreated hair



Result

• Acetyl tetrapeptide-3 stimulates the hair growth activity 3 times more than minoxidil.

In Vitro Effect on Inflammation and IL-8 reduction

Objective

Quantify the decrease of IL-8 production, a pro-inflammatory cytokine induced by physiological mediator. Inflammation is a contributing factor in alopecia.

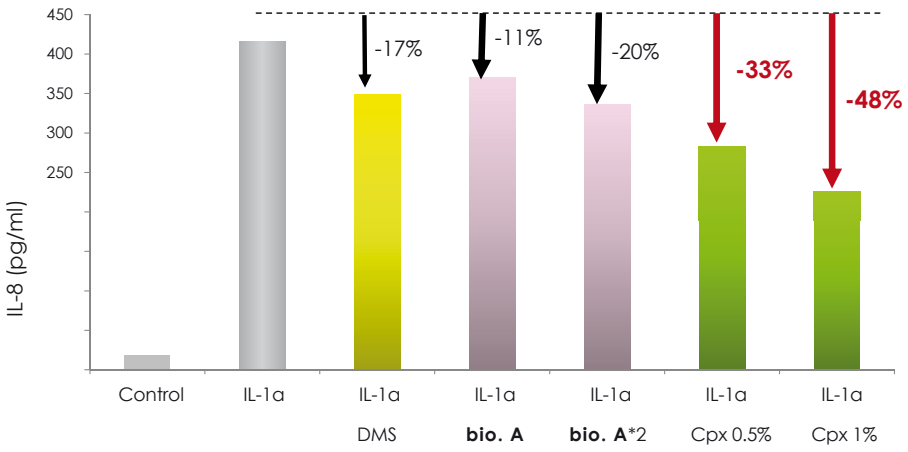
Protocol

• Inflammation was induced in human fibroblasts with IL-1α (physiological mediator)

• Fibroblasts were incubated with or without complex (0.5% - 1%) or DMS (Dexamethasone, positive control) for 24hrs.

• IL-8 quantification using an Enzyme Immuno assay Kit.

IL-8 production by fibroblasts



Result

• The complex decreases pro-inflammatory cytokines with a synergistic and dose dependant action compared to red clover extract alone.

[Acetyl tetrapeptide-3 + biochanin A complex]

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

Objective

Study the capacity of Biochanin A to inhibit the 5-α reductase activity in comparison with a well known 5-α reductase inhibitor EGCG (epigallocatechin gallate a potent antioxidant found in tea).

Protocol

• Assays are based on the measurement of the DHT production from testosterone in presence of either type 1 or 2 human 5 α-reductase.

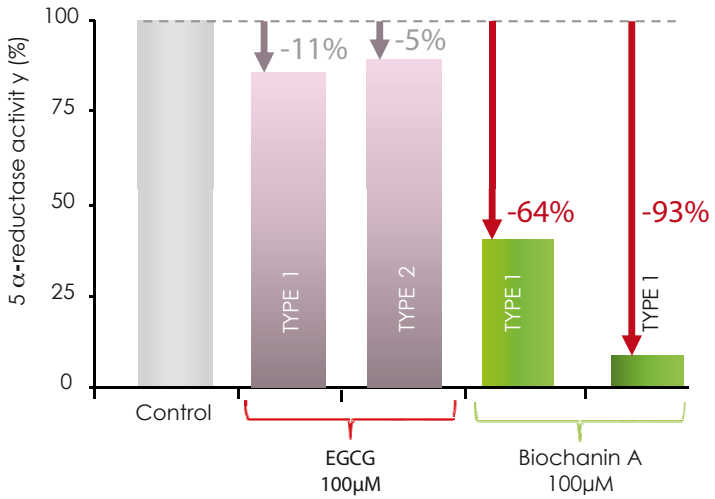
There are 2 forms of enzyme found in the body: type 1 And type 2

5-α reductase

Testosterone > DHT (dihydrotestosterone)

• Testosterone was radio labelled and the amount was determined by TLC (thin layer chromatography) and scanning.

inhibition of α-reductase



Result

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

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

Objective

Quantify the total collagen synthesis induced by Acetyl tetrapeptide-3 on fibroblasts. Hydroxy proline (OH-proline) dosage is a method to assess stimulating capacities of a product on fibroblast collagen production.

Protocol

• Human fibroblasts treated during 7 days with Acetyl tetrapeptide-3 at a 10-7M concentration (≈ 0.016% CapixylTM solution)

• Hydroxyproline dosage is assessed with the Chloramine T reaction and measured by optical density (OD) at 540 nm compared with a range standard

Result

Acetyl tetrapeptide-3 significantly induces the synthesis of hydroxyproline (+35%) and thus increasing collagens synthesis. Acetyl-tetrapeptide-3 stimulates collagen production for better ECM integrity for an optimal hair follicle anchoring.

[Acetyl tetrapeptide-3 + biochanin A complex]

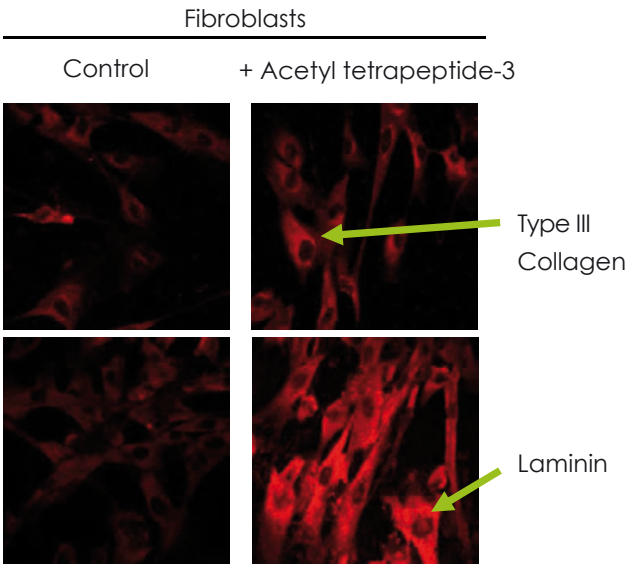
Follicle ECM renewal & Stimulation of anchoring proteins Stimulation of collagen, Collagen III, Collagen VII and Laminin by Acetyl tetrapeptide-3

Objective

Quantify laminin, type III collagen synthesis induced by Acetyl tetrapeptide-3 on fibroblasts. It has been demonstrated that molecules which have an activity on the ECM proteins stimulation, also increase hair follicle size and improve hair anchoring.

Protocol

• Human fibroblasts treated during 3 days with Acetyl tetrapeptide-3 at a 10-7M concentration
• Proteins are detected with specific antibodies linked to a fluorochrome and quantify by confocal microscopy:
• Collagen type III
• Laminin
• Image comparison and fluorescence quantification.



Result

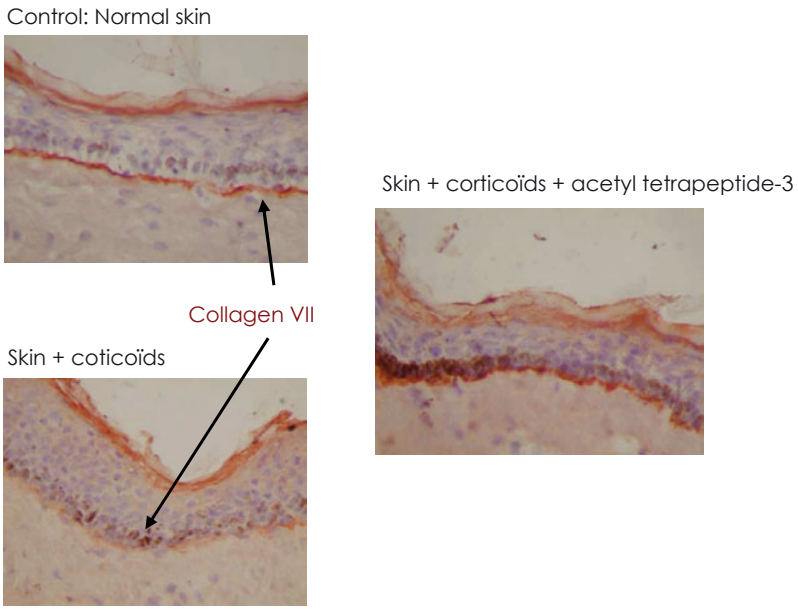
Acetyl tetrapeptide-3 induces the synthesis of laminin (+285%), type III collagen (+65%) in fibroblasts. Acetyl-tetrapeptide-3 stimulates dermal papilla extracellular matrix proteins thus having a direct effect on hair follicle size and better anchoring.

Objective

Quantify type VII collagen synthesis induced by Acetyl tetrapeptide-3 on human skin explants. Collagen VII is a major constituent of the anchoring fibrils and is located in the basement membrane (DEJ) around the papilla.

Protocol

• Human skin explants were pre-treated with dermocorticoïds in order to reproduce natural aging pattern. Dermocorticoids are also known to decrease the hair papilla cells growth.
• Skin explants were then treated during 2 days with Acetyl tetrapeptide-3
• Type VII collagen was detected with specific antibodies and quantify by microscopy • Image comparison and labelling quantification.



Result

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

[Carcinine + functional organic silicium]

Name: Decarboxy carnosine HCL, dimethylsilanediol salicylate
Effect: Hair regrowth and fortification
The complex of organic silicon and carnosine stimualtes the hair growth, improves the hair density and the quality of the hair.
Source:
Carcinine is an identical to a natural component obtained chemically by decarboxylation of carnosin. It has strong anti-oxidant properties and protects the skin against external stress factors to avoid inflammation process and ECM degradation.
The organic silicium is obtained by mild hydrolysis of the dimethylsilyl salicylate leading to biogically active silanol, rich in hydroxy functions and offering a specific response due to the presence of the salicylic radical.
Vectorisation: none
Dosis in F-HAIR MEN: 3.9%

Clinical efficacy on androgenic alopecia

[Carcinine + functional organic silicium]

1 - INTRODUCTION

1.1 - HAIR PHYSIOLOGY

Hair is considered as epidermic appendix and therefore, displays the same essential characteristics that cutaneous epidermis, although with some modifications in their expression.

Hair is secreted from the hair follicle, a part of the epidermis, anchored into the derm.

Hair is constituted of :

- the bulb : it the root of the hair, made up of the hair matrix and dermic papilla.

This part of the hair is fundamental as it is the zone where intense multiplication and keratinocytes differentiation takes place, it penetrates into the connective tissue and is highly vascularized. It provides the elements necessary to make up the hair. If it is destroyed, the follicle sleeves, the hair pipe and the sebaceous gland do not grow any more.

- Follicle sheaths
- The hair shaft, the properly so-called hair
- The sebaceous gland

100 000 to 150 000 hairs can be found but this varies with sex, age or else during a therapy. Other parameters are also involved : seasons parameters, racial, particular physiological conditions like pregnancy or lactation. The hair life is constituted of about 25 cycles divided into 3 main phases :

- Anagen phase : it is characterized by an intense metabolic activity in the bulb : keratine and melanine are synthesized in big amount and the hair grows.
- Catagen phase : it is characterized by the stop of the matricial cells mitotic activity. Hair does not grow any more, follicle starts to atrophy while below, the dermic papilla generates the birth of a new hair.
- Telogen phase : a new hair grows. It pushes into the hair canal the former hair that drops.

THE HAIR IN FIGURES :

- Total number of hairs : between 100 000 and 150 000
- Average density : 250 to 300 hairs/cm2
- Anagen phase (growth) : 90% of the hair during 2 to 6 years, 1 to 2 cm growth per month
- Catagen phase (rest) : 1 to 1,5% of the hair during 2 to 3 weeks
- Telogen phase (drop) : 8,5% of the hair during 2 to 3 month. - Hair lost per day : 50 to 100

1.2 - ALOPECIA (HAIR-LOSS)

Above the normal daily hair-loss (50 to 100 hairs per day), the hair-loss is considered as abnormal and referred to as alopecia. Alopecias are multiple, acute or progressive, congenital or acquired; localized or diffuse.

Pathological states that can be seen are for example : scar alopecia further to a dermatosis, alopecia areata which characterizes secondary syphilis, frontal liminary alopecia, mucinous alopecia of Pinkus (follicular mucinosis), male seborrhoeic alopecia or androgenic alopecia.

Parapharmacy and cosmetology can intervene on the two last alopecias, but with more evidence on the androgenic alopecia.

Besides the pathological states, different factors can modify hair growth cycle.

The pilary cycle is hormone-dependent : testosterone is in situ converted into 5 dihydroxytestosterone (DHT) by the 5 α-reductase enzyme. DHT stimulates the follicle activity, therefore the pilary cycle. This is the reason why alopecia problems are found more often among men than women.

With time, i.e age, papilla activity decreases and hair growth slows down. As growth rate decreases, those falling are not replaced so quickly. In this particular case, cosmetic treatments give interesting results.

Studies have introduced the rigidification of the collagen surrounding the roots of the hair as an essential parameter in alopecia. Originally flexible, collagen can, when it is mature, and under the effect of various stress or oxidative damages, become rigid. This rigidification results in the premature reject of the hair toward outside. It is then replaced by another one, thinner, that cannot correctly settle down into the derm because the rigid collagen prevents it.

[Carcinine + functional organic silicium]

1.3 - ANTI-ALOPECIA ACTIVE INGREDIENTS

Based on the above mentioned causes of alopecia, an active ingredient, designed as anti- alopecia, must both improve the general state of the connective tissue to the root, improve the multiplication of the primary keratinocytes located in the dermic papilla but also avoid or minimize the rigidification of the collagen fibbers.

1.3.1 - Derivatives of organic silicon
The derivatives of organic silicon (SILANOLS) are known for their activity on the cutaneous connective tissue. They prevent from cutaneous aging in restructuring the connective tissue in which silicon is a natural structure element. Many studies evidencing the interest of SILANOLS against cutaneous aging were published.

S ILANOLS also have cytostimulating properties, evidenced on fibroblasts or keratinocytes cultures. The cytostimulant effect takes place in direct contact between the cells and the active (addition of SILANOL in the cell culture medium) but also by cell communication between keratinocytes and fibroblasts (addition of SILANOL in a culture medium of keratinocytes whose secretions are placed on contact with cultured fibroblasts).

Besides, preliminary studies on healthy volunteers had demonstrated the interest of high concentration SILANOLS in the treatment of alopecia and this is the reason why a technique to synthesized a high concentration Silanol was developed : SILANEDIOL SALICYLATE.

1.3.2 - Pseudodipeptides
One of the essential parameters of the hair-loss being the rigidification of the collagen fibbers surrounding the hair root, it is important to prevent this phenomenon mainly caused by the oxidative cross-linking of the proteins.
DECARBOXYCARNOSINE HCL is a anti-oxidant pseudodipeptide for which many studies, performed in our laboratories and in collaboration with universities, evidenced the efficacy in preventing the oxidative cross-linking of the collagen fibbers.

This pseudodipeptide, mainly developed for its activity as reductant of fatty acids hydroperoxides, is largely used as anti-oxidant and anti-aging in skin-care products but this property entirely conforms to the requirements expected in the preventive treatment of alopecia.

2 - PERFORMER OF THE STUDY
The double-blind study was realized on healthy volunteers in order to evidence the efficacy on androgenic alopecia of SILANEDIOL SALICYLATE associated to DECARBOXYCARNOSINE HCL in a lotion.
The clinical study was realized by ALLERGISA DERMATOLOGICAL AND COSMETIC STUDY LTD. Campinas, Brazil, under the responsibility of a dermatologist and received the approbation n°001/99 from an Ethical Research Committee.

3 - P ANEL OF VOLUNTEERS
22 male volunteers, displaying an hereditary androgenic alopecia, at its initial state, and whose trichogram revealed at least 25% of the hair in non-anagen phases were selected. None of these volunteers showed any dermatological disease.
11 volunteers (Group I) were treated by lotion containing the active ingredients and 11 volunteers (Group II) were treated with a placebo (same lotion without actives).

4 - DURATION OF THE STUDY
The study lasted 6 month.

5 - TESTED PRODUCT
The tested product is a hydroalcoholic lotion, containing 25% of ethyl alcohol, 0.70% of DECARBOXYCARNOSINE HCL and SILANEDIOL SALICYLATE.

[Carcinine + functional organic silicium]

6.1 - MATERIAL

- Regular optical microscope
- Glass blades and coverslips
- Surgical needle-holder
- Micropore® adhesive tape
- Entellan® fixer
- Dermatological loupe
- Electronic Digital Caliper Series 727
- Kodak® Digital Science DC210 camera

6.2 - PROCEDURES

Before the beginning of the study, the hair was sampled (according to the here below sampling procedure) and counted ; the sampling zone was marked off and photographed.

The volunteers, selected as described in the chapter 3., were asked not to wash their hair during 4 days before the original collection. Strands of 50 to 100 hairs were sampled from the parietal region close to the vertex and the contralateral region. The strands were rolled and secured to the base with adhesive tape. The distal portion was fixed with a needle-holder and the hair was rolled in the body of the needle-holder near the scalp. The hair was removed with a movement perpendicular to the scalp using the fingertip of the other hand as a support to the scalp. The hair removed was fixed on a glass blade and coverslip for further analysis. A trichogram was then performed in order to evaluate the number of anagen and no- anagen hair.
Besides, 2 areas were selected : one in the occipital region and the other in the parietal region, both with 1 cm2, which was submitted to depilation with a shaving blade. Next, the areas were duly marked and photographed.
The volunteers were instructed to use the products (standard shampoo and hair conditioner, hair lotion and the placebo hair lotion).
The volunteers were instructed to apply enough lotion to massage the scalp twice a day, on dry hair or after washing
A monthly control is operated by the coordinator of the study.
At the end of the six-month study, a new count was made in areas marked off at the beginning of the test, in order to asses hair density.
The volunteers were asked not to have their hair cut during the whole study.

7 - RESUL TS

7.1 - TRICHOGRAMS

Trichograms allow to evaluate the percentage of hairs in anagen phase and those in non- anagen phases.

T ABLE 1 : GROUP I (Active lotiuon)

	ANAGEN PHASE		NON-ANAGEN PHASES	
N°	INITIAL	FINAL	INITIAL	FINAL
1	43 %	80 %	57 %	20 %
2	15 %	75 %	85 %	25 %
3	48.4 %	85 %	51.6 %	15 %
4	55.6 %	75 %	44.4 %	25 %
5	50 %	80 %	50 %	20 %
6	32 %	57 %	68 %	43 %
7	36 %	72 %	64 %	28 %
8	50 %	75 %	50 %	25 %
9	62.5 %	78 %	37.5 %	22 %
10	47 %	72 %	53 %	28 %
11	44 %	75 %	56 %	25 %

[Carcinine + functional organic silicium]

TABLE 2 : GROUP II (Placebo)

	ANAGEN PHASE		NON-ANAGEN PHASES	
N°	INITIAL	FINAL	INITIAL	FINAL
1	50 %	70 %	50 %	30 %
2	55 %	60 %	45 %	40 %
3	30 %	71 %	70 %	29 %
4	40 %	74 %	60 %	26 %
5	46 %	82 %	54 %	18 %
6	43 %	57 %	57 %	43 %
7	62.5 %	77 %	37.5 %	23 %
8	25 %	60 %	75 %	40 %
9	46 %	80 %	54 %	20 %
10	57 %	59 %	43 %	41 %
11	50 %	79 %	50 %	21 %

7.1.1 - Distribution of the hair in anagen and non-anagen phases at the beginning and the end of the study

In the case of healthy hair and for volunteers not suffering of alopecia, the average percentage of hair in anagen phase is about 90% and about 10% in non-anagen phases.

TABLE 3 : AVERAGE DISTRIBUTION OF HAIR ACCORDING TO ANANGEN AND NON-ANAGEN PHASES.

TREATMENT	TIME	HAIR IN ANAGEN PHASE	HAIR IN NON-ANAGEN PHASES
-	BEGINNING	44%	56%
ACTIVE	END	75%	25%
PLACEBO	END	70%	30%

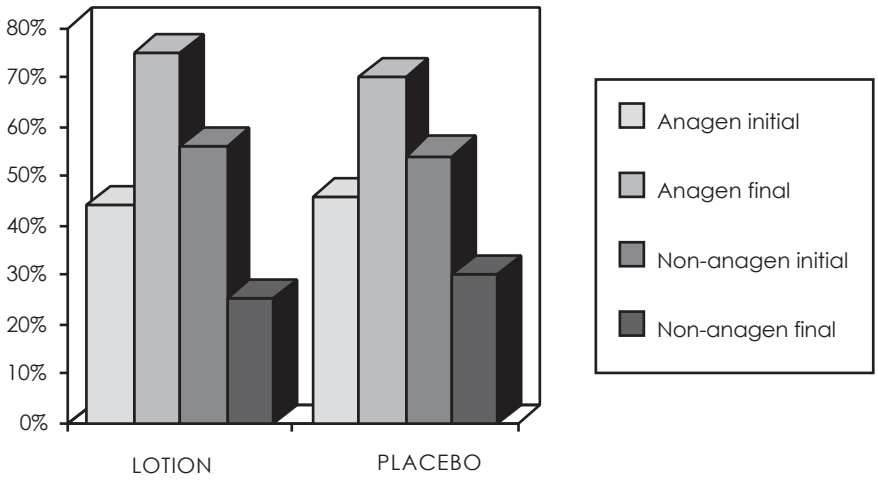
TABLE 4

INCREASE OF THE NUMBER OF HAIR IN ANAGEN PHASE :
- ACTIVE : + 70%
- PLACEBO : +60%

TABLE 5 :

DECREASE OF THE NUMBER OF HAIR IN NON-ANAGEN PHASES :
- ACTIVE : - 55%
- PLACEBO : -46%

GRAPH 1 : AVERAGE DISTRIBUTION OF THE HAIR ACCORDING TO ANAGEN AND NON-ANAGEN PHASES.



[Carcinine + functional organic silicium]

The above tables and graphs show that the volunteers, before the beginning of the treatment have 15 to 62.5% of hair in anagen phase, with an average around 45%. The hair, in non-anagen phase, represent at the beginning 37.5 to 85%, with an average around 55%.

At the end of the treatment, the number of hair in anagen phase varies from 57 to 85%, with an average around 75%, that is to say 70% more than at the beginning of the treatment.

Besides, the number of hair in non-anagen phases, at the end of the treatment, decreased since 15 to 43% of hair is counted in non-anagen phases, with an average around 25%, that is to say 55% less than at the beginning of the treatment.
Some placebo effect was noted, yet minor to that of CAPILLISTIN, since 60% more hair was counted in anagen phase and 46% less in non-anagen phases.

7.1.2 - Ratio of the hair in anagen phase / non-anagen phases

The ratio of hair in anagen phase / non-anagen phases is characteristic of the health of the hair. The higher this ratio, the healthier the hair.

$$R = \frac{\text{Hair in anagen phase}}{\text{Hair in non-anagen phases}}$$

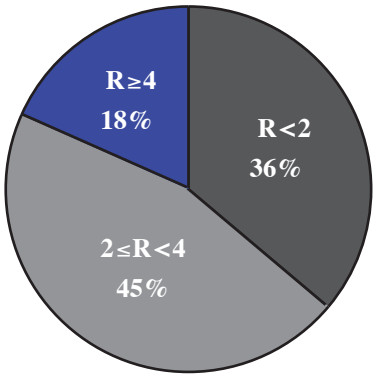
Hair was shared into 3 categories at the beginning and the end of the treatment :
- R<2 : mediocre hair
- 2≤R<4 : healthy hair
- R≥4 : very healthy hair

TABLE 6 : DISTRIBUTION OF THE VOLUNTEERS ACCORDING TO THE RATIO OF HAIR IN ANAGEN PHASE OVER HAIR IN NON-ANAGEN PHASES (R).

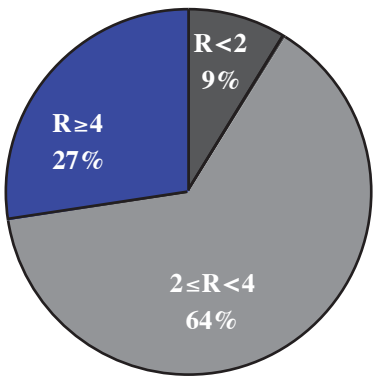
TREATMENT	TIME	R<2	2≤R<4	R ≥ 4
-	BEGINNING	100%	0%	0%
PLACEBO	FIN	36%	45%	18%
ACTIVE	FIN	9%	64%	27%

GRAPH 2 :

VOLUNTEERS USING THE PLACEBO



VOLUNTEERS USING ACTIVE LOTION



[Carcinine + functional organic silicium]

Table 6 shows an improvement with both treatmenst providing that 100% of the volunteers displayed a ratio R<2 at the beginning of the study while they are still 36% in the case of the placebo and only 9% in the case of active lotion.

On the other hand, 64% of the volunteers treated with active lotion show a ratio R comprised between 2 and 4, and 27% of them show a ratio R higher than 4 (against respectively 45% and 18% for the volunteers treated with placebo).

7.2 - CAPILLAR DENSITY

The capillar density represent the number of hair per surface unit.

At the beginning and the end of the 6 month study, a count of the hair on previously marked off areas, is performed in order to evaluate the capillar density.

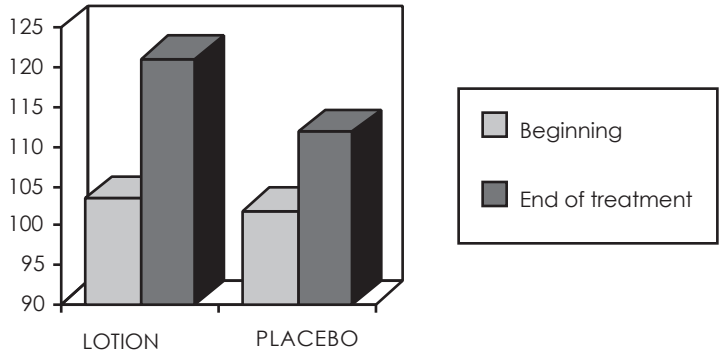
T ABLE 7 : CAPILLAR DENSITY GROUP I (ACTIVE LOTION)

	INITIAL	FINAL
1	114	135
2	113	121
3	90	115
4	94	142
5	85	104
6	119	116
7	104	124
8	91	117
9	96	110
10	103	147
11	128	102

T ABLE 8 : CAPILLAR DENSITY GROUP II (PL ACEBO)

	INITIAL	FINAL
1	82	126
2	112	115
3	113	101
4	102	109
5	96	109
6	104	119
7	104	112
8	96	114
9	98	89
10	95	122
11	120	114

GRAPH 3 : AVERAGE CAPILLAR DENSITY



Graph 3 shows that the average capillary density reached 121 hairs per surface unit, for the volunteers treated with CAPILLISTIN, while it is only 114 for volunteers treated with the placebo.

The parameter A, characteristic of the capillar density of each volunteer between the beginning and the end of the treatment, can be defined :

$$A = \frac{\text{"Nbre of final hairs"-"Nbre of initial hairs"}}{\text{"Nbre of initial hairs"}}$$

[Carcinine + functional organic silicium]

T ABLE 9 : IMPROVEMENT OF THE CAPILLAR DENSITY

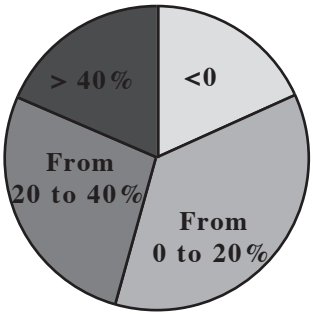
	GROUP I (ACTIVE LOTION)	GROUP II (PLACEBO)
1	18 %	54 %
2	7 %	3 %
3	28 %	-11 %
4	51 %	7 %
5	22 %	14 %
6	-3 %	14 %
7	19 %	8 %
8	29 %	19 %
9	15 %	-9 %
10	43 %	28 %
11	-20 %	-5 %

The volunteers can be shared into 4 categories according to the rate of improvement of their capillar density :
- Degradation : A≤0
- Slight improvement: 0≤A<20 %
- Good improvement: 20 %≤A<40 % - Very good improvement : A≥40 %

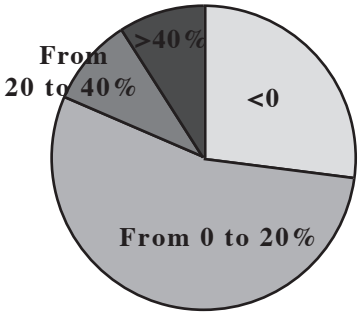
TABLE 10 : DISTRIBUTION OF THE VOLUNTEERS ACCORDING TO THE IMPROVEMENT OF THEIR CAPILLAR DENSITY

	GROUP I (ACTIVE LOTION)	GROUP II (PLACEBO)
A ≤ 0	18 %	27 %
0≤ A<20 %	36 %	55 %
20 % ≤ A<40 %	27 %	9 %
A ≥ 40 %	18 %	9 %

GRAPH 4 : DISTRIBUTION OF THE VOLUNTEERS TREATED BY ACTIVE LOTION ACCORDING TO THE IMPROVEMENT OF THE CAPILLAR DENSITY



GRAPH 5 : DISTRIBUTION OF THE VOLUNTEERS TREATED BY THE PLACEBO ACCORDING TO THE IMPROVEMENT OF THE CAPILLAR DENSITY



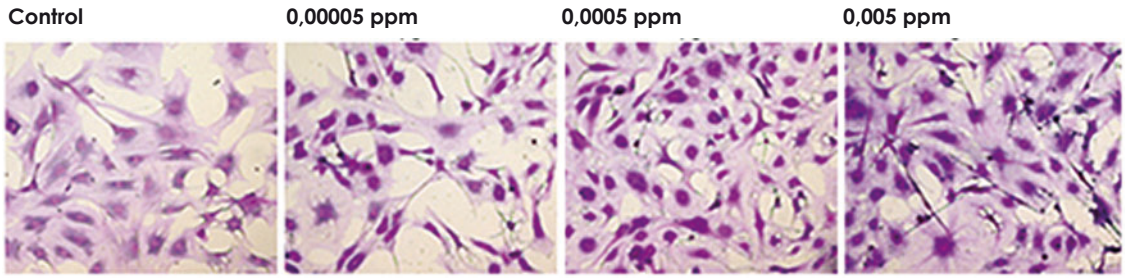
82% of the volunteers treated with active lotion see their capillar density improve when only 73% of the volunteers treated with the placebo.
Moreover, the improvement noticed for the volunteers treated with active lotion is more important as 45% of the volunteers show an improvement higher than 20% in comparison with only 18% for the volunteers treated with the placebo. Among these clear improvements, twice more volunteers treated with active lotion showed an improvement higher than 40%.

8 - CONCLUSION
- the number of **hairs in anagen phase** between the beginning and the end of the treatment **increased of 70%,**
- the number of **hairs in non-anagen** phases between the beginning and the end of the treatment **decreased of 55%,**
- whereas 100% of the volunteers showed a ratio "number of hairs in anagen phase / number of hairs in non-anagen phases" lower than 2, only 9% of them show this weak ratio at the end of the treatment and 27% of them have reached a ratio of 4, characteristic **for a very healthy hair,**
- an improvement of the **hair density** has been observed with **82% of the volunteers** treated with the active lotion.

[CG-αFGF GROWTH FACTOR]

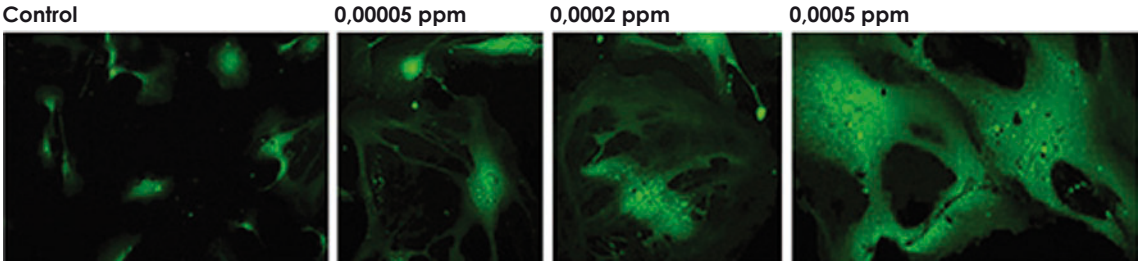
Name: Rh-polypeptide-11
Effect: Hair growth
Strong antioxidant that reduces free radicals and inhibits the hair discoloration. Strongly stimulates the hair growth.
Source: E.coli
Vectorisation: nanosome
Dosis in F-HAIR MEN: 0.05 ppm

Clinical trials
Stimulates the cell proliferation of primary hair cells up to 310% after 72 hours at a concentration of only **0,005 ppm (=5ng/ml)**.



Cell morphology changed after 72 hours of incubation with CG-αFGF on primary hair cell in the condition of serum free medium.

Improves the microcirculation network by stimulating the proliferation of human vein endothelial cells up to 135% after 72 hours at a concentration of only **0,0005 ppm (=1ng/ml)**.

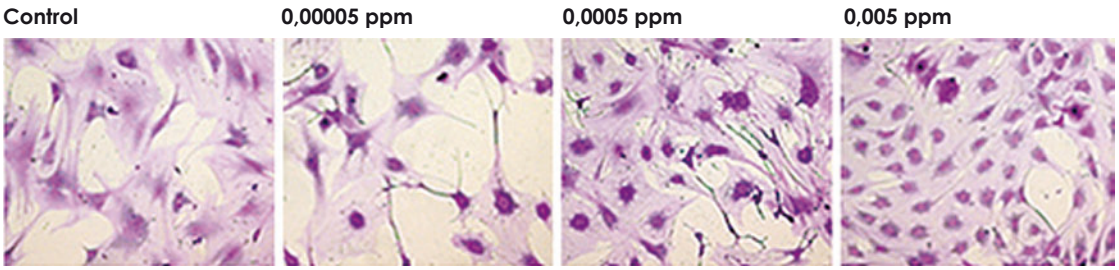


Observing CG-αFGF treated in various concentrations on cell morphology shown a significant changes compared to the control. Cells have stretched our and transformed into a solid shape.

[CG-VEGF GROWTH FACTOR]

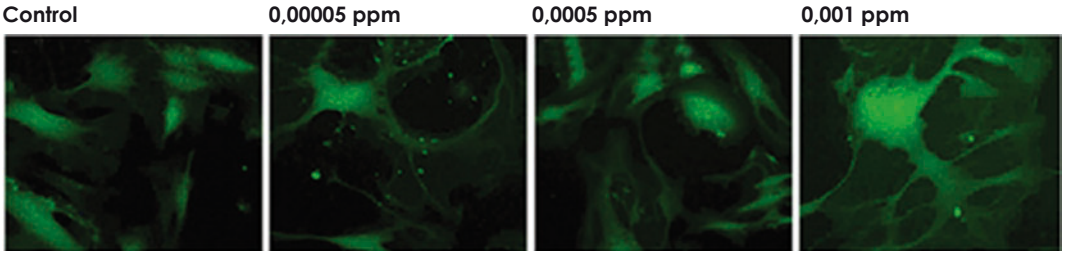
Name: Rh-polypeptide-9
Effect: Hair growth
Hair growth stimulation through the facilitation of nutrient feeding to hair follicle by the VEGF-induced angiogenesis.
Source: E.coli
Vectorisation: nanosome
Dosis in F-HAIR MEN: 0.05 ppm

Clinical trials
Stimulates the cell proliferation of primary hair cells up to 170% after 72 hours at a concentration of only **0,005 ppm (=5ng/ml)**.



Cell morphology changed after 72 hours of incubation with CG-VEGF on primary hair cell in the condition of serum free medium.

Improves the microcirculation network by stimulating the proliferation of human vein endothelial cells up to 138% after 72 hours at a concentration of only **0,001 ppm (=1ng/ml)**.



Observing CG-VEGF treated in various concentrations on cell morphology shown a significant changes compared to the control. Cells have stretched our and transformed into a solid shape.

[CG-COPPER PEPTIDE]

Name: Copper tripeptide-1
Effect: Anti-hair Loss
Delivery of copper peptide to the base of follicles helps strengthen hair while stimulates hair follicles to produce strong hair shaft. Help blood circulation in the scalp and revitalizing hair follicles. Improves hair transplant success
Source: Chemical synthesis
Vectorisation: nanosome
Dosis in F-HAIR MEN: 5 ppm

[CG-IDP2]

Name: Decapeptide-4
Effect: Anti-hair Loss
Delivery of copper peptide to the base of follicles helps strengthen hair while stimulates hair follicles to produce strong hair shaft. Help blood circulation in the scalp and revitalizing hair follicles. Improves hair transplant success
Source: Chemical synthesis
Vectorisation: nanosome
Dosis in F-HAIR MEN: 5 ppm

Clinical trials
CG-IDP2 has Similar Activities Compared to Its Intact Growth Factor, it stimulates the cell proliferation with keratinocyte and fibroblast cells

The cell proliferation is doubled after 72 hours at a concentration of only **1 ppm (=1000 ng/ml)**.

[D-panthenol]

Name: D-panthenol
Effect: Anti-hair Loss
Panthenol is a humectant, emollient and moisturizer. It binds to the hair shaft coats the hair and seals its surface, lubricating the hair shaft and making strands appear shiny.
Source: natural
Dosis in F-HAIR MEN: 0.2%