



BioLetDAge CS



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BioLetDage CS-Line

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What is BioLetDage CS?



- BioLetDage CS System (BLDA) is autologous skin reverse-aging regimen.
- BLDA reinforces cosmetic mesotherapy with its potential benefits at its best without complications.
- BLDA contains the world-first hGH, PRL, hPL & VIP by Regeron, as well as generic ones like EGF & FGFs (see Power Ingredients for more details)
- BLDA adopts combinatorial formulations of proprietary growth factors.
- BLDA stabilizes all and every bioactive growth factors of scientific evidence-based CS-formulations
- Therefore BLDA is not an option but a must for reverse-aging mesotherapeutic skincare.

(Mesotherapy : Esthetic skin treatments using microneedle rollers or other devices to help efficient penetration of cosmetic actives into proper skin layers.)



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BioLetDAge CS-Line

CS-B / Brightening

CS-R / Renewal

CS-W / Anti-wrinkle

CS-S / Anti-irritation

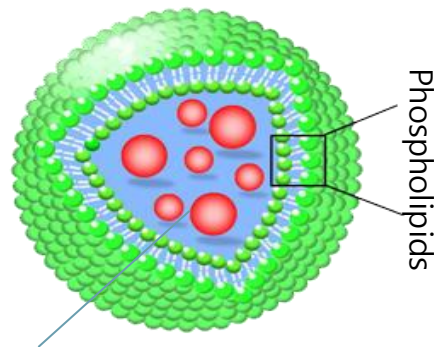
CS-A / Anti-blemish

CS-T / Hair care

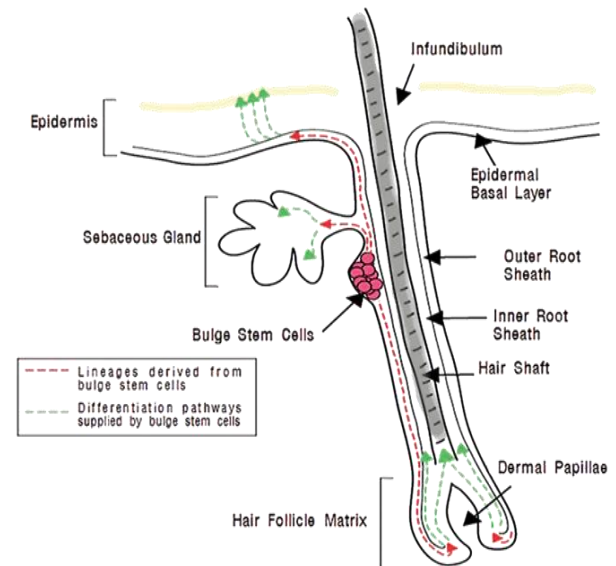
Mechanism (DDS)

- Nanoliposome-encapsulated growth factors (NL-GF) enters skin hair follicles.
- NL-GF inside follicles disintegrates to release growth factors and phospholipids.
- Released growth factors somehow activates follicular skin stem cells.
- Activated follicular stem cells proliferate, migrate and differentiate into various cell-types of the outer skin.
- NL-GF may also activate fibroblasts in the inner skin via a signal transduction mechanism.

Nanoliposome diameter: 200nm



Growth factors
(hGH, Prolactin, Lactogen, VIP, etc.)



(Ref: PNAS 100, 11830)



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Power ingredients

- **NanoClaire-GY** - Our seminal skincare ingredient carrying synthetic human growth hormone(hGH) (INCI: Sh-Polypeptide-7) inside nano-liposome carrier. It is the world-first cosmetic hGH with patented cosmetic applications for improving various skin conditions. NanoClaire-GY gratifies general skincare needs including skin-renewal, anti-sunburn, anti-inflammation, and skin-elasticity.
- **Nanolipo-hGH** - Hair care version of NanoClaire-GY; It shows pro-hair-growth as well as anti-hairloss effects.
- **NanoClaire-LY** - Our another world-first skincare ingredient carrying synthetic prolactin(PRL) (INCI: Sh-Polypeptide-28) inside nano-liposome carrier. NanoClaire-LY showed anti-wrinkle effects in a double-blinded cosmetic clinical test.
- **NanoClaire-AI** - Our another world-first synthetic placental lactogen(hPL) (INCI: Sh-Polypeptide-40)-containing version of NanoClaire-family of ingredients. This patent-pending skincare ingredient showed anti-skin irritation effects in a cosmetic clinical test conducted on the skin of atopic dermatitis patients.
- **Clairesome-VIP** - Our proprietary synthetic vasoactive intestinal peptide(VIP) (INCI: Sh-Polypeptide-65)-containing cosmetic ingredient with local circulation-enhancing effects on the skin. It may well have hairloss prevention as well as skin revitalization effects.
- **Clairesome-EGF** - Our own synthetic epidermal growth factor(EGF) (INCI: Sh-Oligopeptide-1)-containing version of Claioresome-family of cosmetic ingredients.



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In vitro Safety Evaluation of NanoClaire-GY

METHOD:

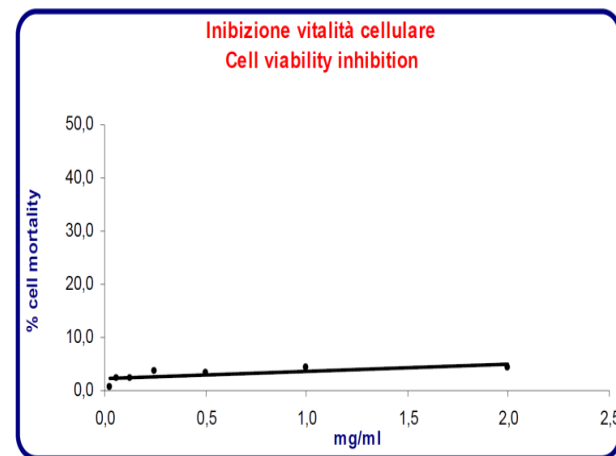
Cultured cells were treated with serial dilution of the active ingredient (2mg/ml down to 0,03 mg/ml) for 24h + 4h. Treated cell viability was calculated and compared to untreated cells (positive control)

Experimental results:

- ✓ No toxic effect
- ✓ No irritating potential

Test Result

Concentrazione Concentration (mg/ml)	Vitalità cellulare % % Cell viability	Inibizione % vitalità cellulare % cell viability inhibition
0,00	100,00	0,00
0,03	99,47	0,53
0,06	97,69	2,31
0,13	97,73	2,27
0,25	96,22	3,78
0,50	96,67	3,33
1,00	95,82	4,18
2,00	95,51	4,49



Source: Farcoderm data processing



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BioLetDAge CS-Line

CS-B / Brightening

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Similar in vitro safety results as NanoClaire-GY had been obtained with NanoClaire-LY, -AI, and Clairesome-VIP.

Endotoxin level of every BioLetDAge CS-line product is below that of EU limit imposed on solution for needle injection.



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BioLetDAge CS-Line

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- CS-T / Hair care

CS-B (Brightening) Proposed Effects

BioLetDAge-CS-B by Regeron is a unique combinatorial formulation for skin-brightening needs.

Key ingredients of BioLetDAge-CS-B :

Sh-Polypeptide-7, 28, and 65 (hGH, Prolactin, VIP), Sh-Oligopeptide-1(EGF) and Niacinamide with pigmentation-reducing effects for skin-brightening in addition to skin-revitalization needs.

Strong Benefits :

- Prevents abnormal skin pigmentation
- Increases vitality and width of the skin epithelium
- Prevents & reverses signs of skin aging caused by lackluster pigmentation



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CS-B (Brightening) Clinical Test

Effect of NanoClaire-GY on skin-brightening

Efficacy of NanoClaire-GY-containing cream on skin-brightening



NanoClaire-GY lightens skin pigmentation and restores skin liveliness



About BioLetDAge

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BioLetDAge CS-Line

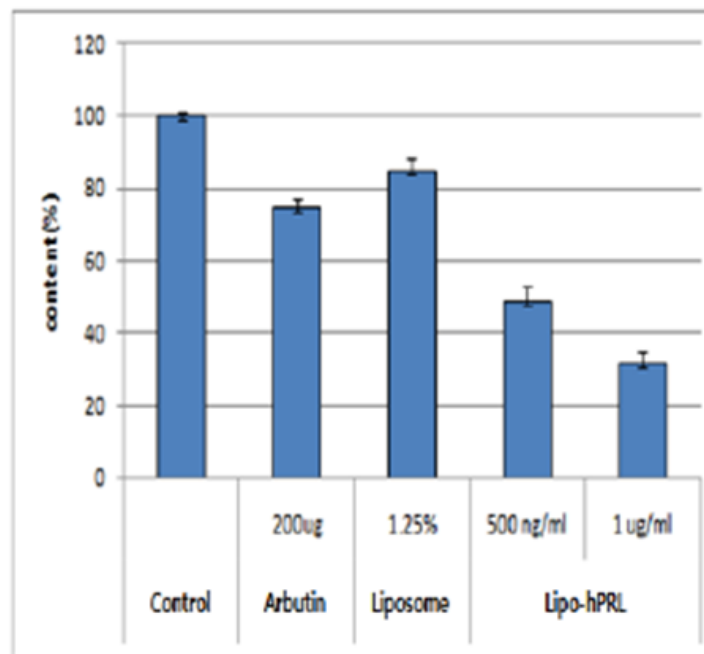
- ▶ CS-B / Brightening
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CS-B (Brightening)

In vitro Test

Suppression of skin pigmentation by NanoClaire-LY

NanoClaire-LY suppresses melanin production of mouse melanoma cell-line (B16F10)



	Melanin Content (%)	S.D
Control (0ng/ml)	100	2.2
Arbutin (200ug/ml)	74.6	3.1
Liposome (1.25 %)	85	3.5
Lipo-hPRL (500ng/ml)	48.6	4.5
Lipo-hPRL (1ug/ml)	31.7	3.0



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BioLetDAge CS-Line

CS-B / Brightening

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CS-A / Anti-blemish

CS-T / Hair care

CS-R (Skin Renewal / Revitalization)

Proposed Effects

BioLetDAge-CS-R by Regeron is a unique combinatorial formulation catering to skin-rejuvenation needs.

Key ingredients :

Sh-Polypeptide-7, 28, 40, and 65 (hGH, Prolactin, Placental lactogen, and VIP), Sh-Oligopeptide-1(EGF), and Niacinamide for optimum skin renewing/revitalizing actions

Strong Benefits :

- Improves renewal of skin epithelial cells
- Rejuvenates aging-skin
- Reduces appearance of wrinkles
- Improves skin elasticity & vitality



About BioLetDAge

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BioLetDAge CS-Line

CS-B / Brightening

► CS-R / Renewal

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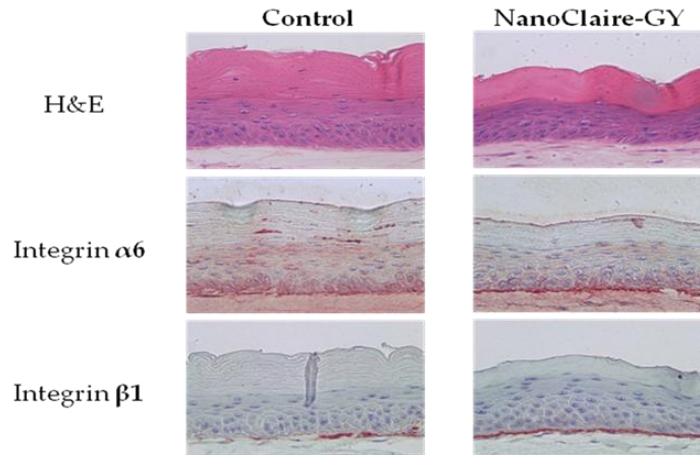
CS-A / Anti-blemish

CS-T / Hair care

CS-R (Skin Renewal / Revitalization)

In vitro Test

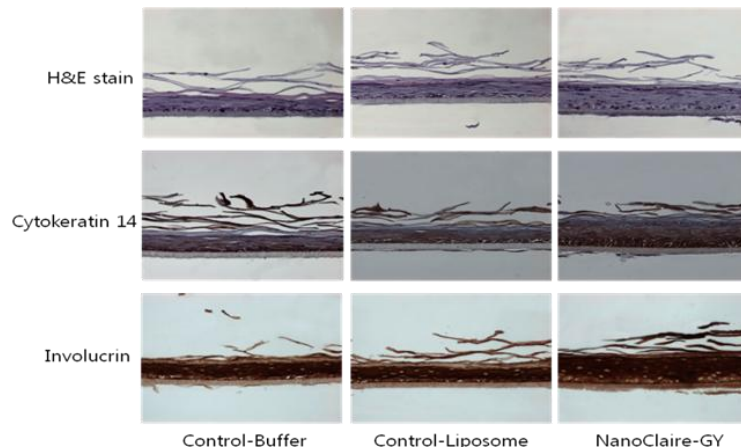
- Effect of Nanolipo-hGH/NanoClaire-GY on Artificial Human Skin (Dermis+Epidermis)



Conclusion:

- Nanolipo-hGH strengthens stem cell characteristics of epidermal basal layer cells.

- Effect of Nanolipo-hGH/NanoClaire-GY on Artificial Human Skin (Epidermis only)



Conclusion:

- NanoClaire-GY treatment on artificial human skin resulted in thickening of epidermis.
- Topical application of NanoClaire-GY suppresses thinning of epidermis that follows aging, thereby help reduce wrinkles and increases skin elasticity.



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BioLetDAge CS-Line

CS-B / Brightening

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CS-A / Anti-blemish

CS-T / Hair care

CS-W (Anti-wrinkle) Proposed Effects

BioLetDAge-CS-W by Regeron is a unique combinatorial formulation for anti-wrinkle needs.

Key ingredients

Sh-Polypeptide-28, 7, and 65 (hGH, Prolactin, VIP)

Sh-Oligopeptide-1(EGF) with clinically proven anti-wrinkle effects

Strong Benefits :

- Reduces the appearance of wrinkles and rejuvenate aging skin
- Stimulate skin cell growth
- Accelerates skin repair and restructuring processes



About BioLetDAge

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BioLetDAge CS-Line

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► CS-W / Anti-wrinkle

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CS-A / Anti-blemish

CS-T / Hair care

CS-W (Anti-wrinkle) Clinical Test



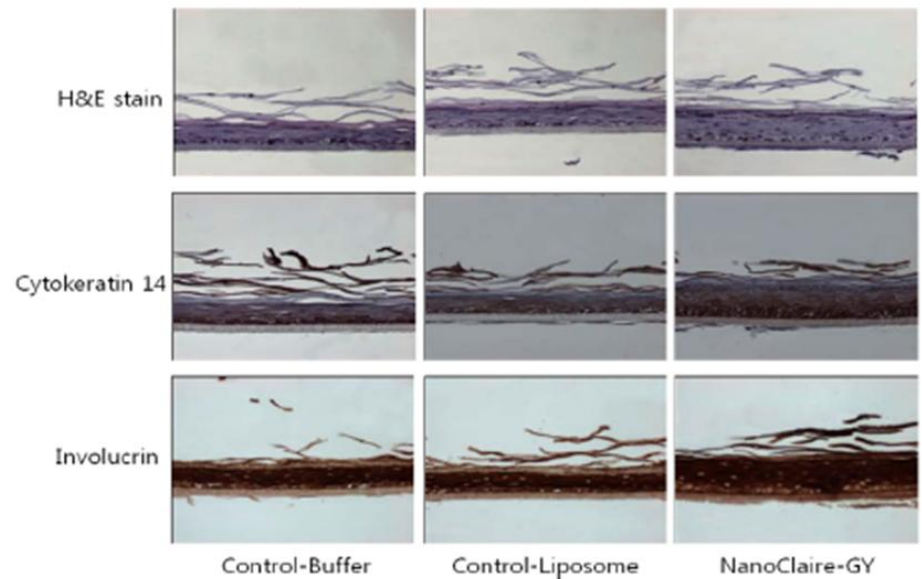
4 WEEKS



8 WEEKS



•Effect of NanoClaire-GY on the Artificial Human Skin (Epidermis only)



Conclusion:

1. NanoClaire-GY treatment on artificial human skin (Keraskin) resulted in thickening of epidermis.

2. Topical application of NanoClaire-GY can suppress thinning of epidermis that follows aging, thereby help reduce wrinkles and increase skin elasticity.



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BioLetDAge CS-Line

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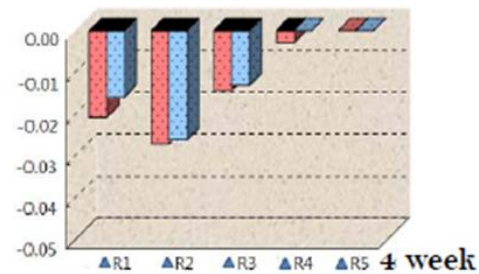
CS-A / Anti-blemish

CS-T / Hair care

CS-W (Anti-wrinkle) Clinical Test

NanoClaire-LY

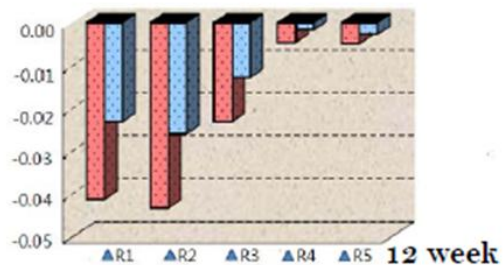
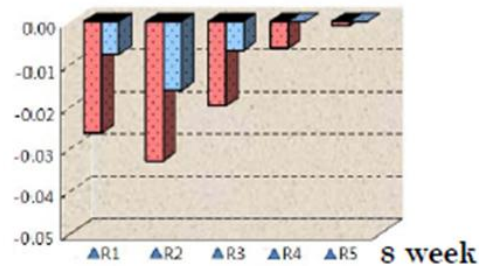
*Efficacy Tests (Clinical)



Imaging Analysis
Results of
R1~R5 on Skin
Replica

Sample A:
containing 2%
NanoClaire-LY

Sample B:
containing
Liposome only
(Control)





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► CS-S / Anti-irritation

CS-A / Anti-blemish

CS-T / Hair care

CS-S (Anti-irritation / atopy)

Proposed Effects

BioLetDAge-CS-S by Regeron is a unique combinatorial formulation with soothing repair actions for skin irritations as well as anti-UV/sunburn damages.

Key ingredients of BioLetDAge-CS-S

Sh-Polypeptide-7 and 40 (hGH and Placental lactogen),

Sh-Oligopeptide-1(EGF) for irritation-prone sensitive skins

Strong Benefits :

- Soothes sensitive skin
- Supression of inflammatory cytokine production
- Improve the skin barrier function
- Strengthens long term moisturizing effects
- Improve the wound healing



About BioLetDage

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BioLetDage CS-Line

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► CS-S / Anti-irritation

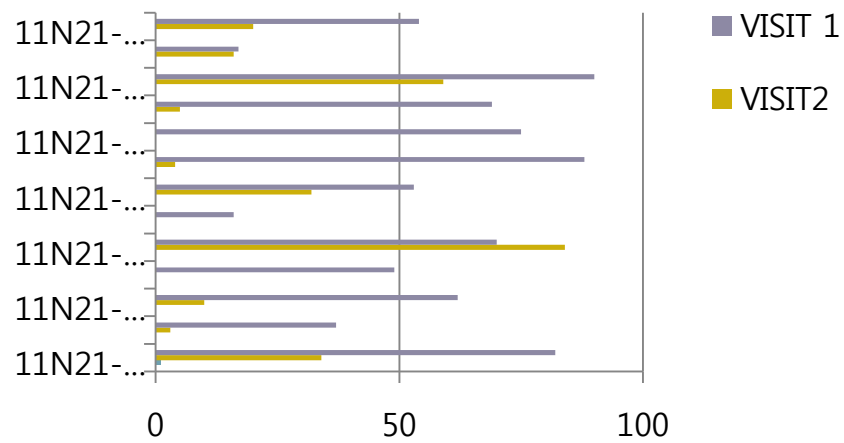
CS-A / Anti-blemish

CS-T / Hair care

CS-S (Anti-irritation / atopy) Clinical Test



Measurement Results of Skin Itchiness





About BioLetDAge

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BioLetDAge CS-Line

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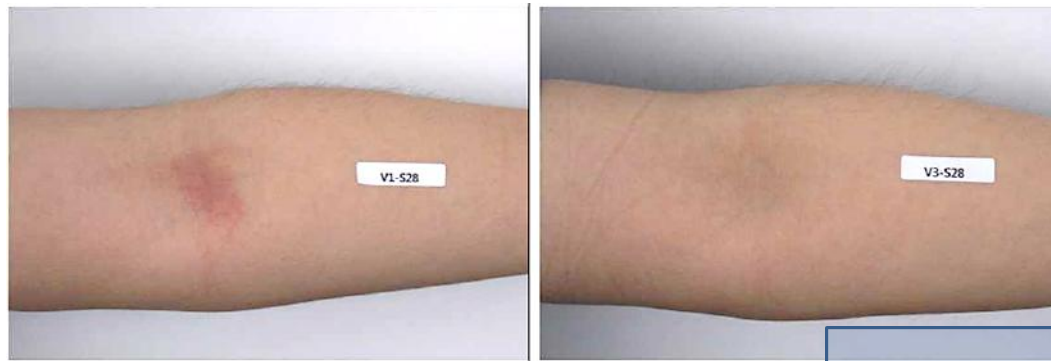
► CS-W / Anti-wrinkle

CS-S / Anti-irritation

CS-A / Anti-blemish

CS-T / Hair care

CS-S (Anti-irritation) Clinical Test

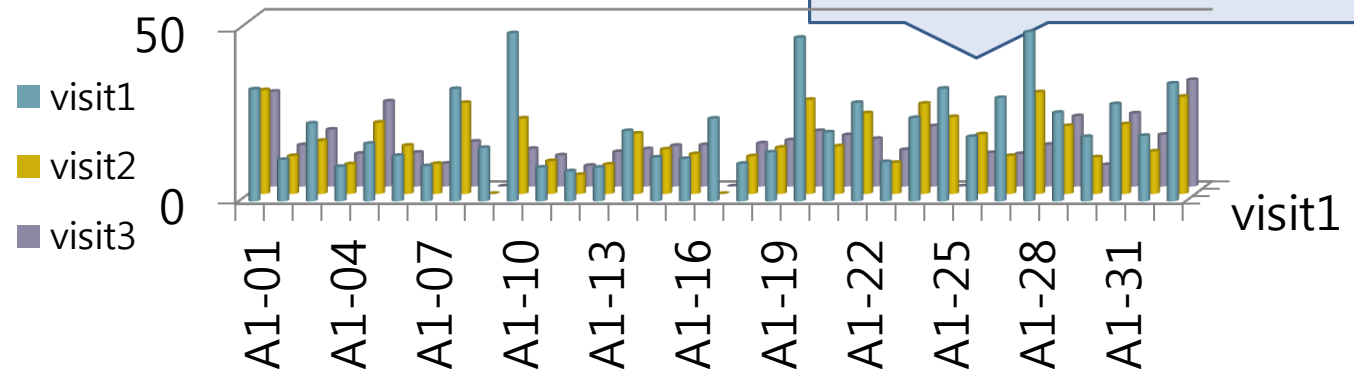


TEWL =
Transepidermal water loss

0 week = 49.1

4 week = 29.5

8 week = 12.1





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► CS-A / Anti-blemish

CS-T / Hair care

CS-A (Anti-blemish)

Proposed Effects

BioLetDAge-CS-A by Regeron is a unique specific combinatorial formulation for anti-blemish/acne needs.

Key ingredients

Sh-Polypeptide-7 and 40 (hGH, Placental Lactogen), Sh-Oligopeptide-1(EGF) and Niacinamide with irritation-soothing and inflammation-suppressing effects for skin blemish/acne.

Strong Benefits :

- Alleviates symptoms involved in acne
- Soothes sensitive skin
- Improves skin barrier function
- Suppresses inflammation



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CS-A / Anti-blemish

CS-T / Hair care

CS-A (Anti-blemish/acne)

Clinical Test

Before



After 1 week



NanoClaire-GY 0.003 mg/ml; we also observed variable degree of anti-acne effect with our finished product-line, NCGY, that contained 2% NanoClaire-GY



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CS-A / Anti-blemish

► CS-T / Hair care

CS-T (Anti-hairloss & pro-hair-growth) Proposed Effects

BioLetDAge-CS-T by Regeron is a unique combinatorial formulation for hair care needs.

Key ingredients

Sh-Polypeptide-7, 28, and 65 (hGH, Prolactin, VIP), Sh-Oligopeptide-1(EGF) and herbal extracts with science- and evidence-based effects for anti-hairloss and hair-growth.

Strong Benefits :

- Prevents hairloss
- Stimulates hair-growth



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► CS-T / Hair care

CS-T (Anti-hairloss & pro-hair-growth) Mechanism

Claresome-VIP

*How it works

Cs-VIPs accumulates around the entrance to the hair follicle

Cs-VIPs move down interacting with the lipids along the hair follicular wall.

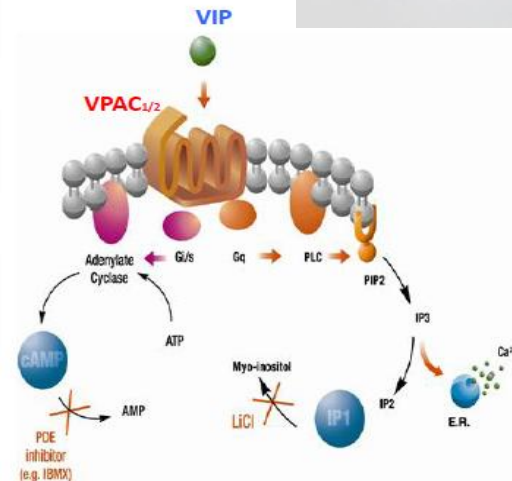
VIPs are released as Cs-VIPs liposome gradually breaks down along the follicular path.

VIPs interact with its receptors (VPAC $\frac{1}{2}$) expressed on the cells of the follicular wall.

The VIP receptors transduce the VIP signals (activated level of cAMP and activation of PKA) into the cell.

These signals may eventually lead to vasodilation of vessel cells in the hair follicle.

Increased supply of O_2 and nutrients to hair follicles may prevent hair-loss and support hair growth.





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CS-T (Anti-hairloss & Pro-hairgrowth) Clinical Test



After 2 weeks



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BioLetDAge CS System

Unique combinatorial formulations of the world-first sh-polypeptides constitutes BioLetDAge CS System by Regeron, the origin of reverse-aging biotechnology.

