Epi-On™

Solution to Skin Recovery

Strengthening Damaged and Weakened Skin Through Epigenetics

Epi-On™

INCI Declaration

Azelamidopropyl Dimethyl Amine (and) Water (and) Butylene Glycol

Benefits

- Accelerate skin repair via epigenetic pathway
- Increase growth factors
- Anti-inflammation
- Anti-bacteria
- Promote cell proliferation

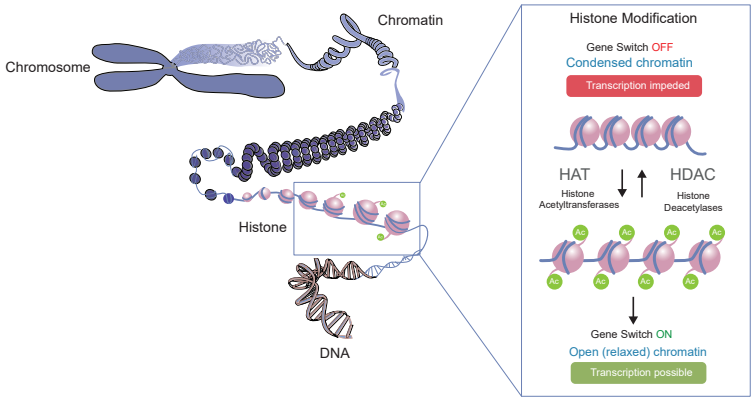
Applications

- Night recovery creams
- Post-acne treatments
- Post-procedure treatments
- After-shave products
- Sun care products

Epi-On™ (INCI: Azelamidopropyl Dimethyl Amine (and) Water (and) Butylene Glycol) is a novel patented active developed with the aim to protect skin against today's harsh environment as well as promote and accelerate skin recovery mechanism through epigenetic regulation.

Epigenetic Mechanism : Histone Modification

Epigenetics is a multitude of "ON-OFF" switches influencing the transcription and translation of genes to proteins without alterations in the DNA sequence. There are three primary epigenetic mechanisms: (1) DNA methylation, (2) miRNA regulation and (3) histone modification, all of which can be potentially induced by developmental, environmental and lifestyle factors. The DNA double helix winds around a special protein known as histone, and this spool complex makes up chromatin which plays an important role in regulating gene expression. Addition of an acetyl group on histone can reduce electrostatic attraction between the histone and the negatively charged DNA backbone, thus loosening the chromatin structure and making it more accessible for active transcription. Studies uncover Epi-On™ as an epigenetic regulator which accelerates tissue regeneration through inhibiting HDAC (histone deacetylase) activity and upregulating the gene expression of growth factors, as well as protects skin against oxidative stress via $H_4K_{16}ac$ (acetylation of histone 4 on lysine 16) alteration. Epi-On™ also imparts anti-inflammatory and anti-bacterial effects to further reinforce the skin recovery process.

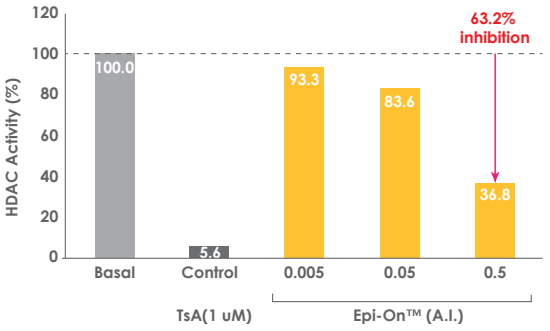


Epi-On™

Efficacy Study

1 Epi-On™ Acts as HDAC Inhibitor

HDAC (histone deacetylase) is a class of enzymes that remove acetyl groups from DNA-wrapped histones, thus altering the chromatin accessibility and interactions that deactivate certain gene transcription as well as downstream cellular functions. HDAC activities tend to increase with biological aging as well as tissue damage. An *in-vitro* HDAC activity assay, using a potent HDAC inhibitor Trichostatin A (TsA) as positive control, was performed on immortalized human keratinocytes cell line HaCaT to demonstrate the capability of Epi-On™ to attenuate HDAC activities in a dose-dependent manner.



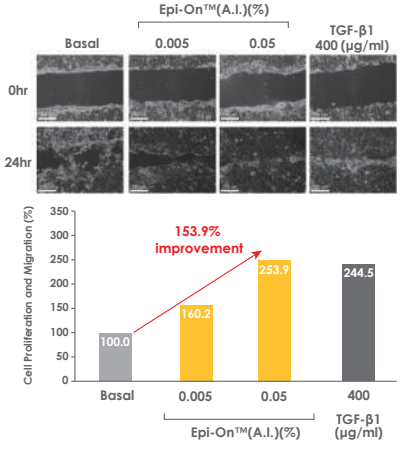
2 Epi-On™ Upregulates Gene Expression of Growth Factors

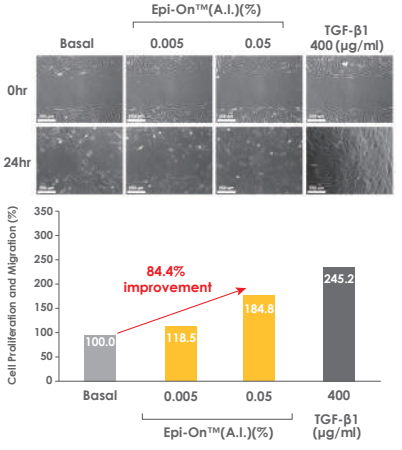
Acting as HDAC inhibitor, Epi-On™ was further investigated using qPCR to demonstrate its ability to upregulate the gene expression of various growth factors (EGF, TGF-β1, TGF-β2, IGF1 and VEGFA) involved in the proliferation and differentiation of keratinocytes and fibroblasts. The table results on the right show that 0.5% (A.I.), Epi-On™ imparts excellent ability to upregulate the expression of these growth factors.

		0.5% Epi-On™(A.I.)	
Cell type		Keratinocytes (HaCaT)	Fibroblasts (Hs68)
Gene Expression of Growth Factors	TGF-β1	↑42%	↑20%
	TGF-β2	↑100%	↑77%
	IGF1		↑71%
	VEGFA		↑43%
	EGF	↑40%	

3 Epi-On™ Promotes Proliferation and Migration of Both Keratinocytes and Fibroblasts

To study the efficacy of Epi-On™ to promote the healing effect in both epidermal and dermal layers, cell migration assays were conducted on two cell types: keratinocyte cell line HaCaT and fibroblast cell line Hs68. The results show that Epi-On™, at use level as low as 0.05% (A.I.), significantly promote the proliferation and migration of both keratinocytes and fibroblasts by +153.9% and +84.4%, respectively. Through epigenetic pathway, Epi-On™ imparts an outstanding property to promote tissue repairing and remodeling in injured monolayer cells.





Efficacy Study

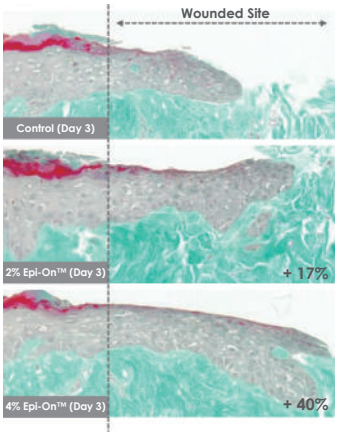
4 Epi-On™ Attenuates Inflammatory Reaction

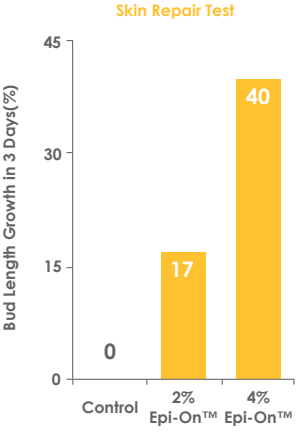
Epi-On™ Attenuates Inflammatory Reaction Inflammation is an early haling phase that take place concurrently with hemostasis where coagulation occurs, and the transition from inflammation to proliferation is a critical step in the skin repair mechanism. Hence, the anti-inflammatory property of Epi-On™ was investigated by measuring the protein levels of two cytokines IL-6 and IL-8, which cause inflammatory responses in weakened or damaged skin, on LPS-treated HaCaT cell line. At 0.5% (A.I) use level, Epi-On™ significantly downregulates the production of IL-6 and IL-8 to 72.7% and 73.5%, respectively, to alleviate inflammatory responses.

Secretion (%)	Basal	Epi-On™ (A.I.) (%)			
		Control	0.125	0.25	0.50
		LPS induced IL-6 & IL-8 secretion on HaCaT cell line			
IL-6	23.3	100	82.7	86.8	72.7 ↓ 27.3%
IL-8	17.7	100	96.0	80.0	73.5 ↓ 27.3%

5 *Ex-Vivo* Study : Skin Repair and Barrier Strengthening Activities

The efficacy of Epi-On™ on tissue repair and skin barrier strengthening activities was evaluated through an ex-vivo study conducted by Laboratories BIO-EC on wounded human skin explants from a 22-year-old Caucasian woman. After staining according to Masson's trichrome, the skin morphology was analyzed, along with the growth bud length of the wounds, on Day 3. The results demonstrate that 2% and 4% Epi-On™ can effectively accelerate the cutaneous healing with significant increase of growth bud length by as much as 17% and 40%, respectively, in just 3 days. Epi-On™ is proven to help promote and strengthen the homeostasis of weakened skin barrier and damaged tissue.



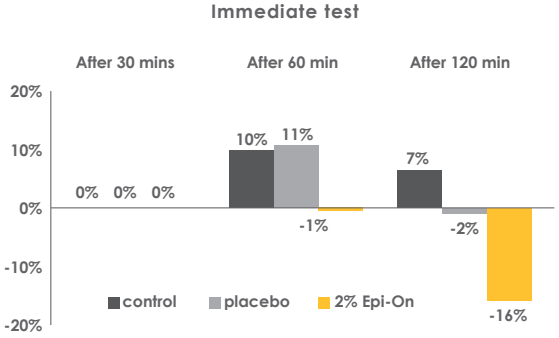


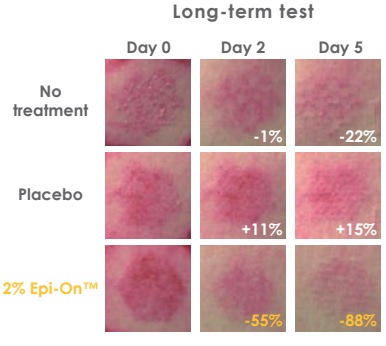
6 *In-Vivo* Study : Skin Barrier Recovery

The efficacy of Epi-On™ on skin recovery was evaluated through two in-vivo studies to research recovery ability of laser ablated skin.

1. Immediate test on 5 Caucasian women with test time : afrer 30 mins, 60 mins and 120 mins.
2. Long-term test on 20 Caucasian women with 4 sensitive skin & 16 normal skin , test time : Day 0, Day 2 and Day 5.

The results demonstrate that 2% Epi-On™ can reduce erythema of the lesions in the both studies.





2% Epi-On™ reduced erythema of the lesions at day 2 and day 5 after laser ablation on sensitive skin.

Epi-On™

Novel Epigenetic Regulator for Skin Recovery & Strengthening

Claim Ideas for Epi-On™

- Promote the strengthening of weakened skin barrier
- Stimulate the repairing of damaged tissue
- Upregulate the expression of growth factors
- Accelerate the cell proliferation and migration via epigenetic pathway
- Anti-inflammation
- Anti-bacteria
- Decrease in facial erythema after treatment

Applications

- Night recovery creams
- Post-acne treatments
- Post-procedure treatments
- After-shave products
- Sun care products

Marketing Benefits

- Patented, novel epigenetic-regulating active
- Excellent water solubility and easy-to-formulate
- Stable, non irritant and safe
- Halal approved

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