

ALISTIN[®]

MULTI-POTENT ANTI-AGING COMPOUND

Anti-glycation
Anti-oxidation
Revitalization

MULTI-POTENT COSMETIC AGENT

Anti-wrinkle
Sun care
Sensitive skin
Body firming

EXSYMOL
MONACO

ALISTIN®

Besides intrinsic aging, the skin is under the constant aggression of oxidative entities (solar radiations, pollution, physical stress, etc.). The resulting oxidative stress can affect the structure of the cutaneous tissue and the metabolic activity of its composing cells such as fibroblasts and keratinocytes. Since these factors are essential for the quality of the skin, Exsymol developed **Alistin**, a peptidic compound which is able to protect the skin components such as the collagen from these aggressions and to maintain the metabolic activities of the exposed cells.

Treatment with **Alistin** will both prevent and **repair** the daily aggressions-induced damages, allowing the skin to remain healthy, firm and beautiful. **Alistin** acts in three different, non-exclusive, ways for a maximal efficiency:

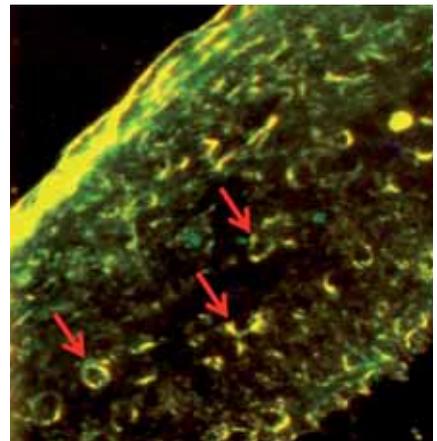
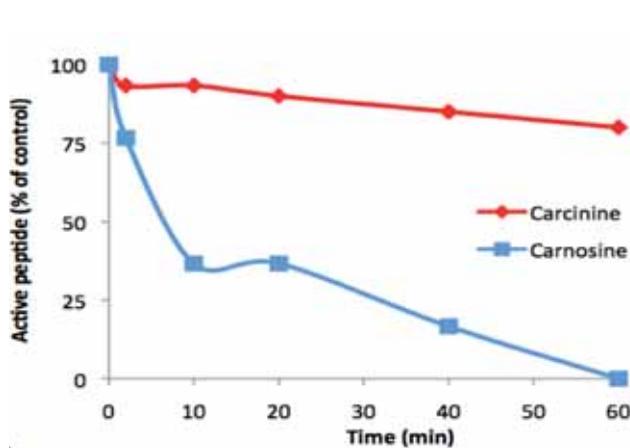
- 1) Anti-oxidation / anti-stress
- 2) Anti-glycation
- 3) Metabolism stimulation

Hence, Alistin protects and/or reduces the noxious effects of an exposure to oxidative stress that can eventually lead to severe damage as shown below:

Cellular level	Skin level
1) Accumulation of oxidative forms Protein alterations (including structural proteins) DNA mutation	Structural collapse, loss of elasticity, fine lines
	Tissue inflammation
	Less efficient dermis tightening activity
2) Protein glycation (including collagen)	Homeostasis loss
3) Slackening of cell metabolism	Dehydration

Exsymol's solution : The decarboxy-carnosine

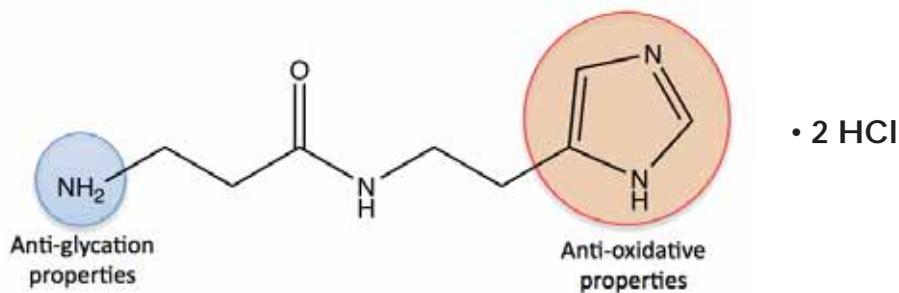
Carcinine (or Decarboxy Carnosine HCL), commercially available as **Alistin**, is a natural peptoid that has been identified as a potent anti-glycant and anti-oxidant. Furthermore, it has the advantage of being relatively stable when in contact with air. Derived from carnosine, another natural anti-oxidative compound, **Carcinine** displays similar anti-oxidative properties while being substantially more stable than its parent compound as shown below. This increased resistance to enzymatic degradation, makes **Alistin** a better candidate than carnosine for *in vivo* and therefore cosmetic applications.



Alistin (→) localizes on keratinocytes membrane as assessed by immuno-histochemistry.

Furthermore, **Alistin** displays good bioavailability and localizes on the cell membrane (e.g. keratinocytes) as shown on human reconstructed epidermis (HRE).

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INCI name: DECARBOXY CARNOSINE HCL

Carnosine is a nature-identical compound obtained from the decarboxylation of carnosine. Carnosine has demonstrated its ability to protect the skin integrity from oxidative stress (by detoxification, scavenging and damage repairing). Carnosine is commercially available as **Alistin** (10% aqueous solution) or **Carnosine 2HCL** (powder).

SKIN BENEFITS

CELL DETOXIFICATION

Peroxidase-like activity (*Babizhayev et al., 1994 - TI_0239*)
Reduction of acid forms threatening the integrity of cells' membrane
Faster DNA recovery after stress (*Exsymol - DO_0751*)
Global scavenger + free radical-induced damages repair (*Exsymol, DO_1044*)

SKIN STRUCTURAL PROTEINS (COLLAGEN) PROTECTION

Anti-glycation activity (*Exsymol - DO_1133*)
Combination of 3 defense mechanisms: competition, detoxification and reverse-glycation (*Exsymol - DO_1133*)

METABOLIC PROTECTION AND STIMULATION

Control of pro-inflammatory cytokine production (*Exsymol - DO_1157*)
Increase of sirtuin expression (*Fréchet et al., 2010 - A3_1295*)
Increase of collagen production rate (*Fréchet et al., 2010 - A3_1295*)

COSMETIC APPLICATIONS

ANTI-GLYCATION AND REVERSE-GLYCATION

ANTI-OXIDATION – Global protection

ANTI-WRINKLE – Deep wrinkles; Smoothness

SUN CARE – DNA protection; Photoaging

BODY FIRING – Increase of collagen production; Contraction of the extra-cellular matrix

REVITALIZATION – On the cellular level; Sirtuin production

SENSITIVE SKIN – Soothing; Free radicals protection; Control of inflammation

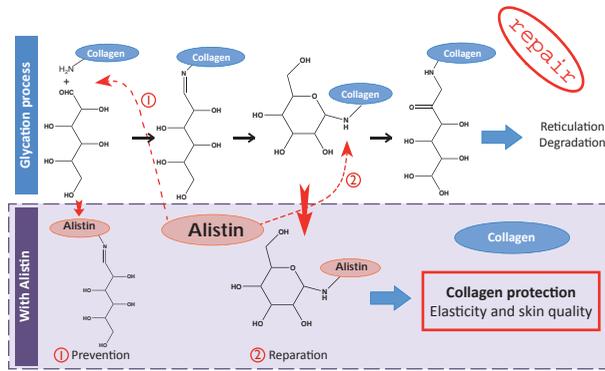
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ALISTIN prevents and repairs cutaneous tissue damage.

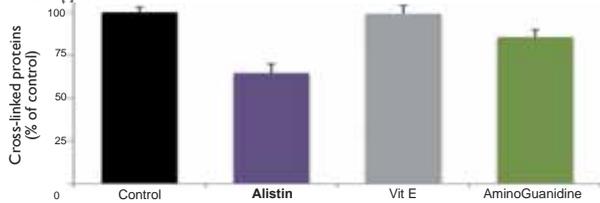
Alistin for anti-glycation

Alistin protects the collagen and other proteins from the glycation processes at two different levels:

- ① **Prevention:** by glucose scavenging.
- ② **Repairment:** by substituting itself to the collagen in a transglycation process.



Hence, **Alistin** prevents the protein from cross-linking, while other anti-oxidants such as vitamin E fail at it. **Alistin** is even more potent than aminoguanidine, a reference in anti-glycation. Furthermore, the final products of the reaction are neither toxic nor mutagenic.



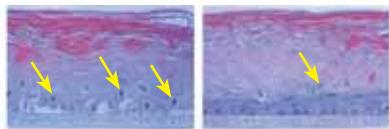
The skin preserves its structure and elasticity

Alistin protects from UV-induced DNA damage

UV radiations cause DNA mutations in epithelial cells.



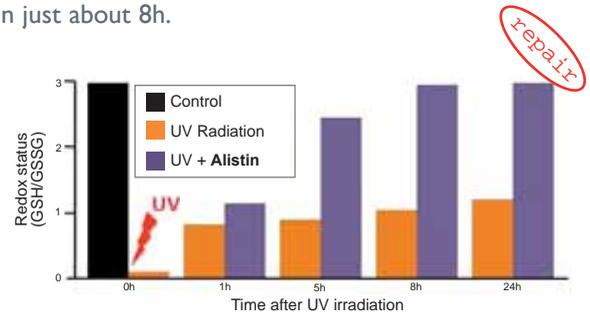
Alistin reduces UV-induced mutations such as TT dimers (→) that might ultimately lead to the formation of apoptotic cells such as sunburn cells (→) as assessed on HRE.



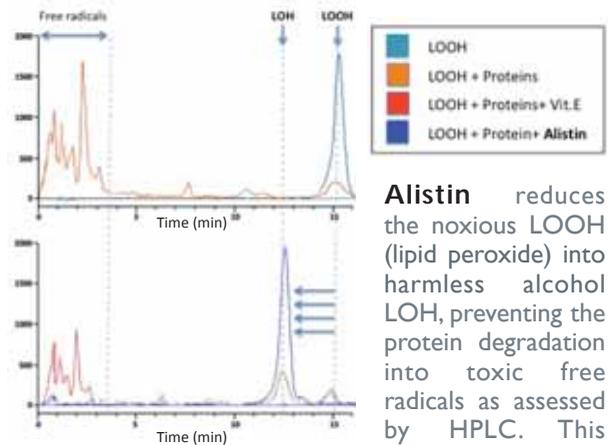
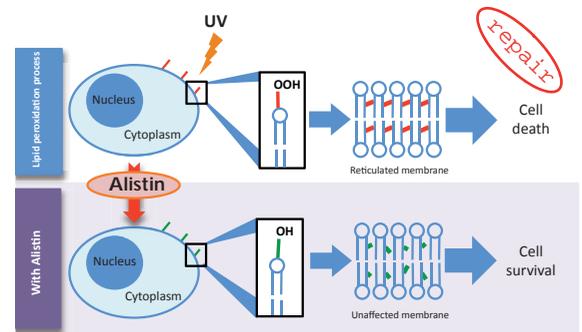
Alistin protects the DNA from UV-induced damage and mutation. **Alistin** stimulates the production of DNA-protecting proteins, hence decreasing the number of apoptotic cells.

Alistin, a unique anti-oxidant

UV radiation can induce damage that can be monitored by measuring the cells redox status. The skin can slowly recover by itself from UV irradiation. However, even after 24h, the self healing process still was not complete. Treatment with **Alistin** led to a full recovery in just about 8h.



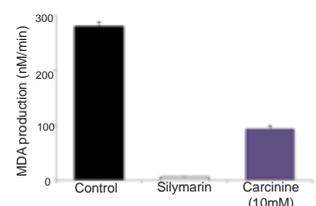
Alistin provides a fast and reliable protection against oxidative stress-induced damage as measured above.



Alistin reduces the noxious LOOH (lipid peroxide) into harmless alcohol LOH, preventing the protein degradation into toxic free radicals as assessed by HPLC. This

anti-oxidative effect is unique and is not shared by other anti-oxidants such as Vitamin E.

Alistin's anti-oxidative properties are also due to its scavenging power as shown by its ability to reduce MDA (a toxic byproduct of oxidative stress) production.



The skin is protected, healthier.

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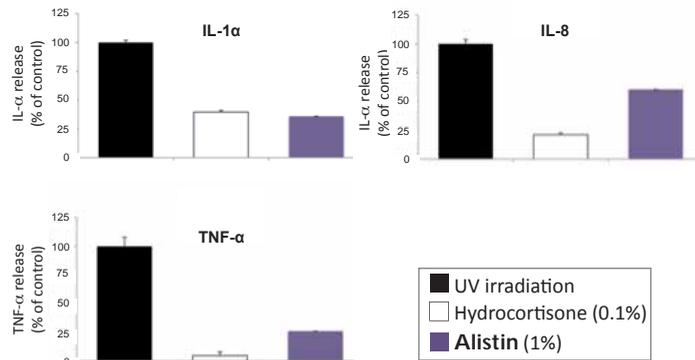
ALISTIN has positive effects on skin cells' metabolism and function.

Alistin reduces skin inflammation

Aggressions can lead to skin inflammation. **Alistin**, when applied on human reconstituted epidermis, reduces the secretion of pro-inflammatory cytokines such as TNF- α , IL-1 α and IL-8.

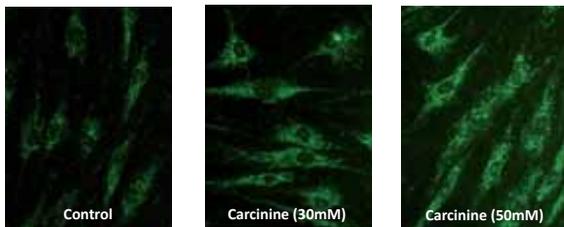
Hence, **Alistin** has anti-inflammatory and soothing properties comparable to corticoids without the severe side effects.

The skin is soothed.



Alistin energizes the skin

Sirtuins are proteins involved in aging, stress resistance and cell metabolism through their ability to maintain ATP levels.

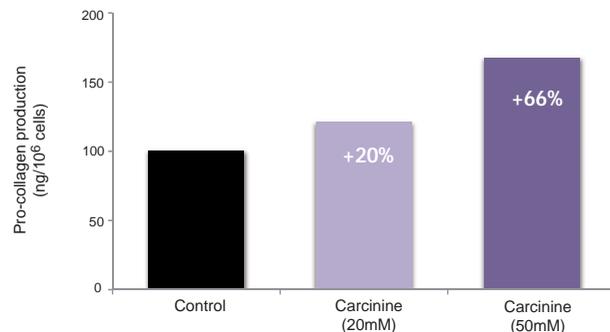


Alistin stimulates the production of sirtuins in a dose dependant manner, hence enhancing skin cells metabolic abilities.

The skin is energized.

Alistin stimulates collagen production

With age, the collagen production is reduced, the firmness of the skin is reduced, wrinkles appear.



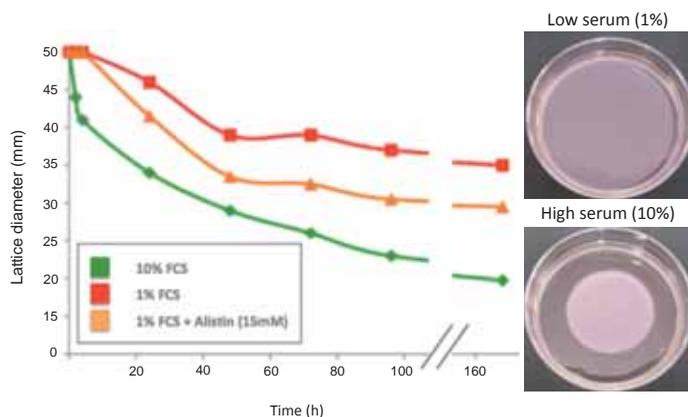
Alistin stimulates fibroblastic collagen production in a dose dependant manner. The skin is denser and younger.

The skin is denser.

Alistin increases skin firmness

With age, fibroblasts' firming abilities decrease. Using collagen lattice, an *in vitro* model of dermis, we measured the ability of primary fibroblasts to contract the collagen fibers. Hence, for fibroblasts in low serum media (1%), representative of an aged dermis, the lattice contraction is much slower than in a high serum media (10%) which is representative of a young dermis.

Treatment of serum deprived fibroblasts with **Alistin** accelerated the lattice contraction, showing that **Alistin** has firming abilities.



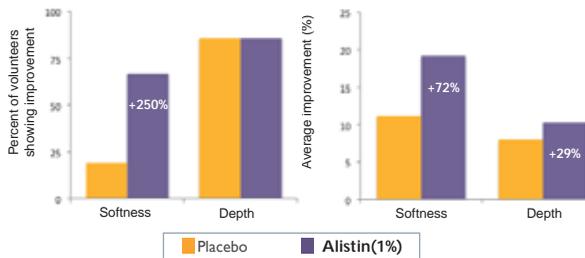
The skin is firmer, younger.

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Realised under dermatological control, these *in vivo* assays were performed on volunteering men and women.

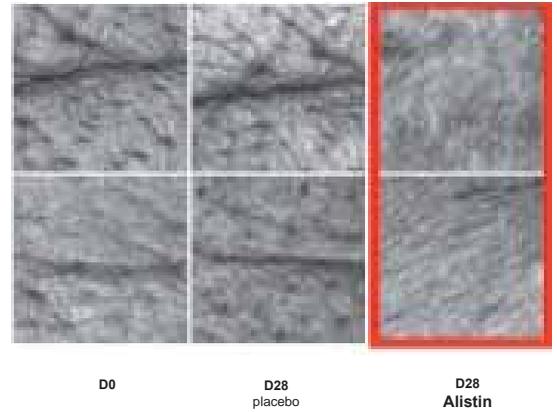
Alistin reduces deep wrinkles

A 28 days treatment with **Alistin** visibly reduced wrinkles. Of the 21 volunteers, 67% showed a visual improvement after the treatment with **Alistin**.



Lip to nose wrinkles

Forehead wrinkles

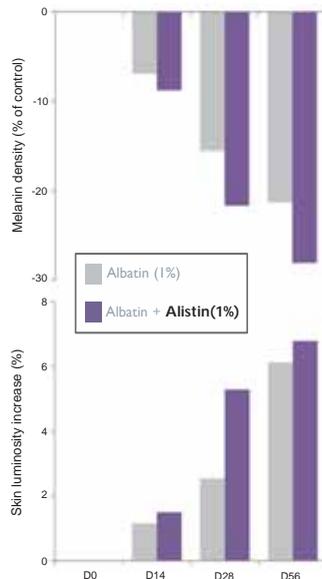


The skin is smoother, softer and visibly younger.

Alistin as a booster for skin tone uniformity

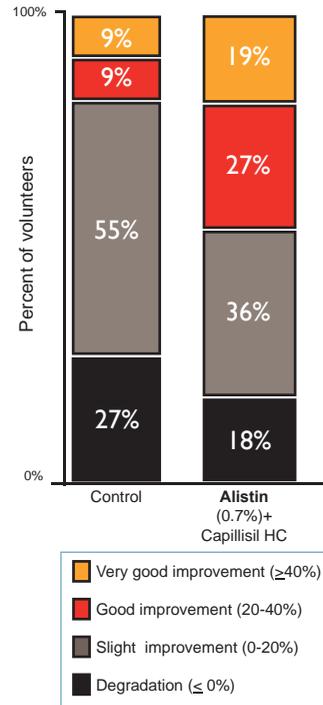
Alistin enhances **Albatin** (a melanogenesis inhibitor) brightening abilities. After 56 days of treatment, volunteers that received the combined treatment displayed a 28% decrease in melanin density and an increase in skin luminosity of about 7%. All these values are higher than the treatment with **Albatin** alone. Hence, by optimizing the effects of the skin brightener **Albatin**, **Alistin**

contributes to the skin tone's uniformity and to the decrease in age spot number and intensity.



The skin is brighter, more uniform.

Alistin improves hair density



By increasing the amount of hair in the anagen phase, a 6 month treatment with **Alistin**, when coupled with **Capillisil HC**, improves the hair density for 80% of tested alopecic men.

The hair is denser, healthier.

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ANALYTICAL COMPOSITION

Decarboxy Carnosine HCL	10% (w/w)
Butylene glycol	8.18%
Preservatives*	
Water	(sq) 100%

TECHNICAL CHARACTERISTICS

Limpid colorless liquid.
pH ≈ 5
Density at 20°C ≈ 1.0
Miscible with water, alcohol and glycols.
Non miscible with hexane, mineral and vegetal oils.

PRESERVATIVES (*)

Different preservative systems are available in order to fit with your requirements. Please contact us for additional details about the available versions.

TOLERANCE & TOXICITY STUDIES

ALISTIN is perfectly tolerated. Tolerance and toxicity studies were performed using both *in vitro* (cell culture and reconstructed epidermis) and *in vivo* (human volunteers) methods.

FORMULATION

Advised doses : 0.5 to 1.5%.
No particular formulation restriction.

AVAILABILITY

ALISTIN is available in 1, 5, 30 and 60 kg drums.
ALISTIN is also available in powder (anhydrous) as **Carcinine 2HCL**.



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