ALISTIN®

MULTI-POTENT ANTI-AGING COMPOUND
Anti-glycation
Anti-oxidation
Revitalization

MULTI-POTENT COSMETIC AGENT
Anti-wrinkle
Sun care
Sensitive skin
Body firming
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:

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

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.

Furthermore, Alistin displays good bioavailability and localizes on the cell membrane (e.g. keratinocytes) as shown on human reconstructed epidermis (HRE).
Carnicine is a nature-identical compound obtained from the decarboxylation of carnosine. Carnicine has demonstrated its ability to protect the skin integrity from oxidative stress (by detoxification, scavenging and damage repairing). Carnicine is commercially available as Alistin (10% aqueous solution) or Carnicine 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-RGLYICATION AND REVERSE-RGLYICATION**

**ANTI-OXIDATION** – Global protection

**ANTI-WRINKLE** – Deep wrinkles; Smoothness

**SUN CARE** – DNA protection; Photoaging

**BODY FIRMING** – 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
ALISTIN®

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:

† Prevention: by glucose scavenging.

‡ **Reparation** 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.

**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 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. **Alistin** stimulates the production of DNA-protecting proteins, hence decreasing the number of apoptotic cells.

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

The skin is protected, healthier.
ALISTIN®

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-1α, 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.

![Control](image1) ![Carclinicine (30mM)](image2) ![Carclinicine (50mM)](image3)

**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.

![Graph](image4)

**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.**
ALISTIN®

CLINICAL RESEARCH: IN VIVO TESTING

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

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 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.

The skin is smoother, softer and visibly younger.

Alistin as a booster for skin tone uniformity

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.
ALISTIN®

**ANALYTICAL COMPOSITION**

<table>
<thead>
<tr>
<th>Component</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decarboxy Carnosine HCL</td>
<td>10% (w/w)</td>
</tr>
<tr>
<td>Butylene glycol</td>
<td>8.18%</td>
</tr>
<tr>
<td>Preservatives*</td>
<td></td>
</tr>
<tr>
<td>Water</td>
<td>(sq) 100%</td>
</tr>
</tbody>
</table>

**TECHNICAL CHARACTERISTICS**

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

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

**PRESERVATIVES (*)**

**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.

Advised doses: 0.5 to 1.5%.

No particular formulation restriction.

**FORMULATION**

ALISTIN is available in 1, 5, 30 and 60 kg drums.

ALISTIN is also available in powder (anhydrous) as Carcinine 2HCL.

EXSYMOL - MONACO