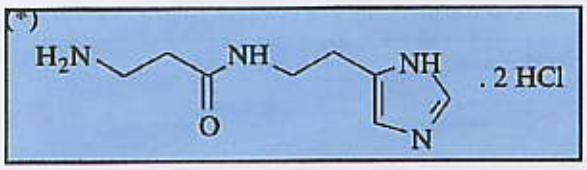
ALISTIN

Hydroglycolic solution (90/10 water : butanediol-1,3)
of 10% CARCININE hydrochloride (*)
INCI Denomination of carcinine : DECARBOXY CARNOSINE HCL

Chemical familly

ALISTIN is a synthetic pseudodipeptide but a REPLICA of NATURAL COMPOUND, of high stability, resistant to enzymatic hydrolysis.



Analytical composition

Carcinine hydrochloride	10,000 g
Butanediol-1,3	8,180 g
Sodium methyl parahydroxybenzoate	0,145 g
Water sq	100,000 g

Technical characteristics

Limpid colorless liquid
pH : around 5
Density at 20° C : around 1
Miscible with water, glycols, alcool.
Non miscible with hexane, mineral and vegetable oils.

Availability

1, 5 or 30 kg drums

Uses

Anti-aging and sun-products

- Preventive action :
ALISTIN counteracts the protein oxydative cross-linking, particularly due to fatty acid hydroperoxydes.

- Repairing action :
ALISTIN reduces and detoxifies the membrane hydroperoxides (REVERSE EFFECT)

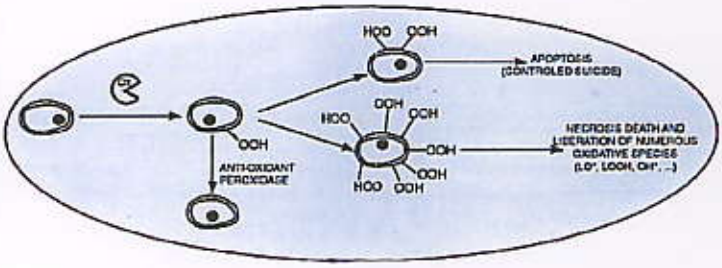
ALISTIN is designed for all kinds of anti-aging products (Creams, gels, lotions, milks...)

ALISTIN can be formulated in day and/or night-care products, in sun-products, including after sun, and for all kinds of skin (in particular for sensitive skin).

BIOLOGICAL ACTIVITIES

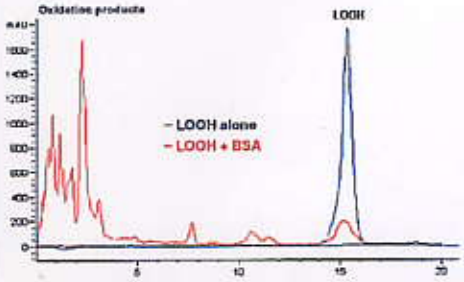
PHYSIOLOGICAL UNIVERSAL ANTI-OXIDANT

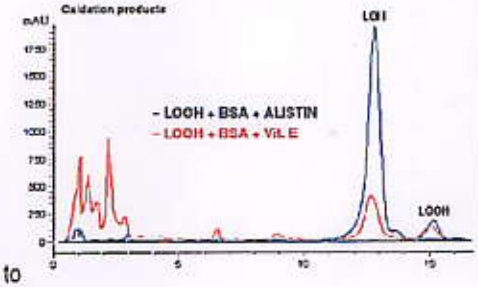
The cell membranes are among the principal targets affected by oxidation which results in the formation of fatty acid hydroperoxides. In the case of a moderate oxidation, enzymes, such as peroxidases, or specific anti-oxidant, such as pseudodipeptides, can reduce the hydroperoxides and repair the oxidative damages. To a more advanced oxidation extent, the cell «self destroys» (apoptosis) in order to interrupt the oxidative cascade. At the final stage, the cell death («necrosis death») induces the liberation of fatty acid hydroperoxides that migrate towards the different compartments of the connective tissue while spreading their dramatic oxidative effects.



REPAIRING OF MEMBRANES

At the cell membrane level, the oxidative stress induces first the phospholipid peroxidation.
In vitro, our model represents the reaction of linoleic acid hydroperoxyde (LOOH) with bovine serum albumin (BSA). The reaction products are analyzed by HPLC (234 nm).





HPLC analysis substantiates the ability of ALISTIN to reduce toxic fatty acids hydroperoxides (LOOH) into non toxic alcohols (LOH). The commonly used lipophilic anti-oxidant, vitamin E, being only capable of scavenging activity, is therefore ineffective once hydroperoxides are formed.

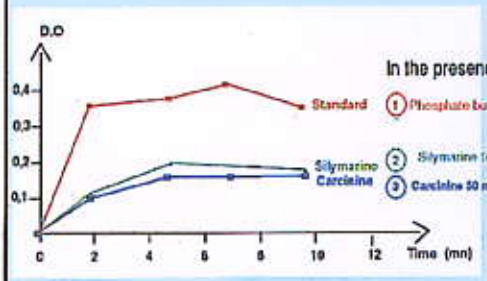
ALISTIN CAN REPAIR THE MEMBRANES

(In vitro study)

ANTI-OXIDANT EFFECT ON CELL MEMBRANE FRACTIONS

Carcinine and carnosine are anti-oxidant endogenous molecules located in the heart, kidneys, muscles, blood plasma... The anti-oxidant effect of carnosine has been established only *in vitro*.
We have evidenced the ability of **ALISTIN** to limit the oxidation reactions in a selected cellular compartment. The anti-oxidant effect was evaluated using the MDA variations after various incubation times.

Cell membranes fractions submitted to an oxydative stress (stimulus = linoleic acid hydroperoxide)



In the presence of :
1. Phosphate buffer (Standard)
2. Silymarine (a mM Reference anti-oxydant
3. Carcinine 50 mM (Alistin)

ALISTIN CAN REPAIR THE CELL MEMBRANES

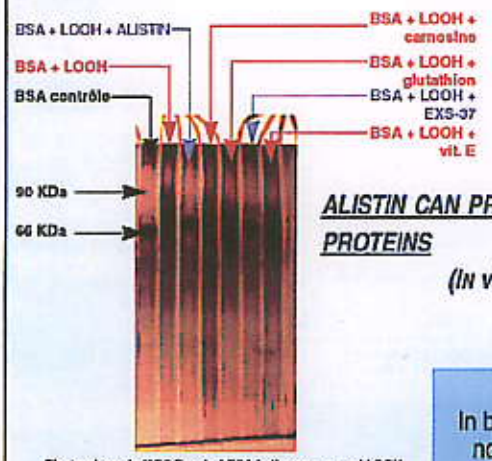
(Ex vivo study)

BIOLOGICAL ACTIVITIES

PHYSIOLOGICAL UNIVERSAL ANTI-OXIDANT

PROTEINS PROTECTION

The phospholipid peroxides spontaneously break down into free radicals and toxic aldehydes. Oxidative stress is spread over from the lipophilic phase (cell membrane) towards the hydrophilic phase, resulting in the oxidation of the surrounding proteins (collagen, SOD...). The subsequent oxidative damages can be evaluated *in vitro* in a medium containing both LOOH or MDA and proteins such as BSA or SOD (natural anti oxidant enzyme). The anti-oxidant properties of various molecules were studied according to that procedure.

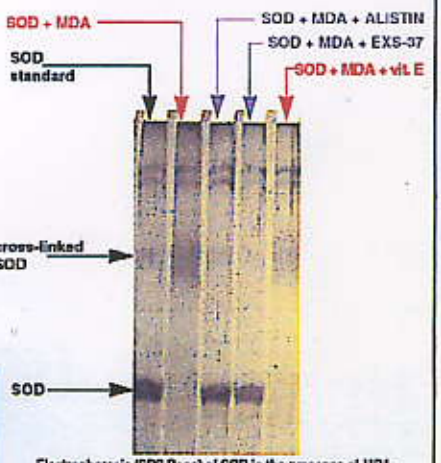


Electrophoresis (SDS Page) of BSA in the presence of LOOH

ALISTIN CAN PROTECT PROTEINS

(In vitro study)

In both cases, no effect of vitamin E is noticed.



Electrophoresis (SDS Page) of SOD in the presence of MDA

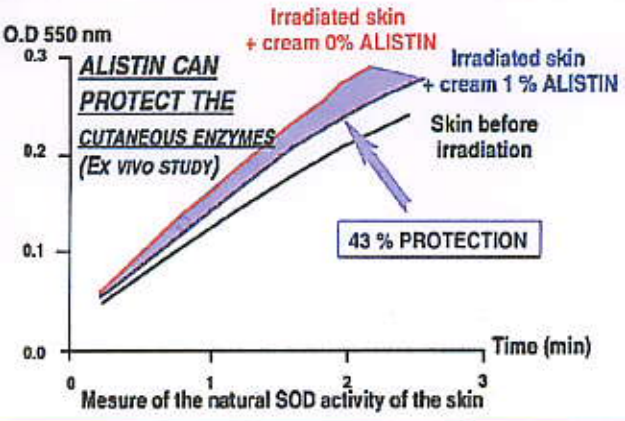
Due to its lipid peroxydase-like property, ALISTIN reduces the fatty acids hydroperoxides and stops any further oxidative propagation. The electrophoresis shows that the surrounding proteins are protected.

ALISTIN also exhibits protecting properties towards proteins (such as SOD) against oxidation due to toxic aldehydes.

PROTECTION OF CUTANEOUS ENZYMES

The protecting effect of ALISTIN on the natural SOD of the skin has been evaluated on a cutaneous fraction (epidermis-derm) irradiated by U.V. (A and B) and measured by the kinetics of the reduction of cytochrome C by $O_2^{\bullet-}$.

This *ex vivo* test shows that a cream containing 1% of ALISTIN preserves 43% of the natural skin anti-oxidant defenses from U.V. induced degradation.



EXSYMOL

BIOLOGICAL ACTIVITIES

PHYSIOLOGICAL UNIVERSAL ANTI-OXIDANT

ANTI-GLYCATION EFFECT

Proteins such as collagen suffer oxidative cross-linking under the effect of toxic aldehydes (such as 4-HNE or 4-hydroxy-nonenal), characterized by a browning of the collagen fibers (see picture) and resulting in a loss of elasticity and premature aging of the skin. An immunoenzymatic quantification of the rate of cross-linking by 4-HNE has evidenced the protecting effect of ALISTIN.

STANDARD COLLAGEN

COLLAGEN CROSS-LINKED BY 4-HNE

The protection properties of ALISTIN agaisnt U.V.-induced damages has also been evidenced. For that, the microscopic observation of the apoptosic cells but also the study of the DNA protection (comet assay) or its fragmentation, and the analysis of the cellular cycle by flow cytometry have been used.

ALISTIN CAN PROTECT DNA

COMET ASSAY

DNA PROTECTION / APOPTOSIS

Tolerance study

Tests carried out *in vivo* evidence that the product is neither toxic nor irritant. These tests consist in studying :

- acute toxicity by oral administration on mice,
- ocular irritation on rabbits,
- primary skin irritation on healthy human volunteers,
- sub-acute toxicity by iterative applications on healthy human volunteers,
- sensitization on healthy human volunteers,
- photosensitization on healthy human volunteers (phototoxicity et photoallergy).

We also studied the tolerance by alternative *in vitro* methods (study of the ocular tolerance potentials) performed on cell culture. The potential of ocular tolerance is evaluated by measuring the cytotoxicity on fibroblasts culture isolated from rabbit cornea.

Formulation

ALISTIN is a very stable hydroglycolic solution (90/10 water : butanediol-1,3). It can be formulated without restriction by addition to the water phase. Advised concentration is about 0.5 to 1.5%.

Existing studies

(available on request)

Technical data

•

Anti-free radical effect on hydrophylic targets

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Anti-free radical and peroxydase effect on lipophylic targets

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Anti-oxidant effect on membranes fractions

•

Anti-inflammatory properties

•

Protection from UV radiations of the skin's natural anti-oxidative defenses

•

Glycation, glycoxidation, toxic aldehydes : interest of Pseudodipeptides

•

Protection of DNA from UV

•

Photoprotection and anti-oxidant properties

•

Tolerances

(acute toxicity, evaluation of the tolerance on rabbits and healthy human volunteers, itemative methods)

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BARNET

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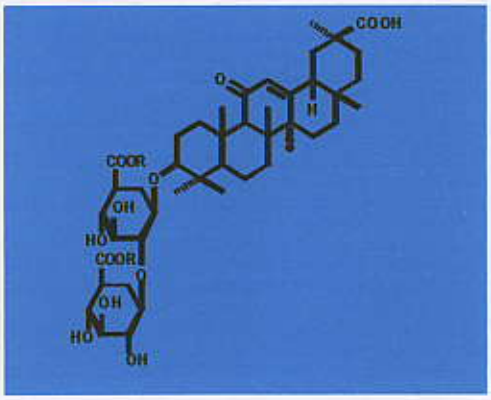
NET-DG

甘草

- Water-Soluble Anti-Inflammatory
- Approved for Quasi-Drug Applications in Japan
- Protector of Hyaluronic Acid

DESCRIPTION

Dipotassium Glycyrrhizinate ($C_{42}H_{60}K_2O_{16}$) is a water soluble active with a molecular weight of 899. It is a natural anti-inflammatory extracted from licorice roots.



PROPERTIES

NET-DG is an anti-inflammatory which can play an important role in formulating today's "sensitive skin" treatments. It has been tested in vitro to demonstrate anti-inflammatory effects, anti-hyaluronidase activity, UV-erythema reduction, inhibition of histamine release, and effect on arachidonic cascade (LTB_4, PGE_2). Anti-inflammatories such as NET-DG are now commonly used as a standard "fourth phase" in Japanese emulsions for skin and hair care.

FORMULATION

NET-DG is a white to faintly yellow crystalline powder with a faint characteristic odor. It is soluble in water and in 50% ethanol. The recommended use level is 0.3 %. This product is stable at pH 5.0 to 11.0.

LEGISLATION

INCI Name: Dipotassium Glycyrrhizinate JMHW: 41-500129
CAS: 68797-35-3 EINECS: 272-296-1

ECOCERT Status: Certified as natural to the ECOCERT Cosmetic Standards.

2009-03-25

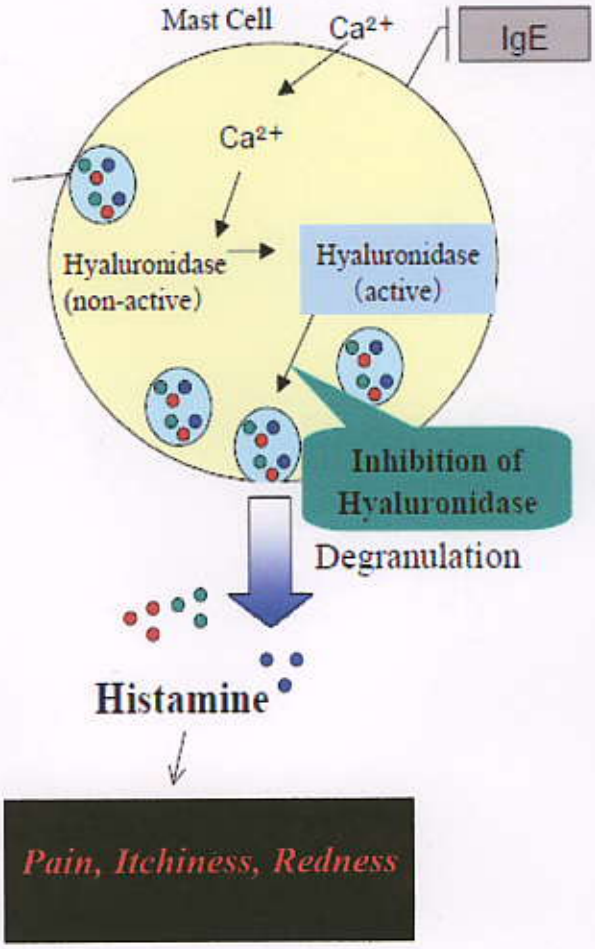
NET-DG

EFFECT OF NET -DG ON HYALURONIDASE ACTIVITY

Hyaluronidase, an enzyme is activated during inflammation, plays a role in the destruction of the connective tissue matrix, and increases the permeability of inflammatory cells and blood vessels.

Inhibition of Hyaluronidase Activity

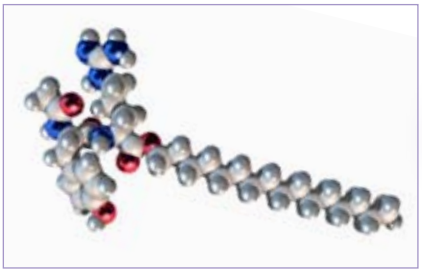
Sample	IC50 (μg/mL)
NET-DG	***3.4***
Cf., Scutellaria Root Extract	***39.0***
Cf., Indomethacin	***20.0***



FACE MAKE-UP

patent pending

IDEALIFT™



N-acetyl-Tyrosyl-Arginyl-O-hexadecyl ester

GRAVITY CONTROL

Function:
Fights against skin sagging and improves resistance to gravity.

Definition:
Idealift™ is composed of 7500 ppm of the lipodipeptide N-acetyl-Tyrosyl-Arginyl-O-hexadecyl ester.

Properties:
Idealift™ not only stimulates elastin synthesis but also promotes a correct and functional elastic fibre architecture by inducing the most important elements involved in tissue structure.

Characteristics:
Idealift™ has already demonstrated its effect on the treatment of sensitive skin.

Points of interests:
This peptide sequence is based on the dipeptide Tyr-Arg which is naturally present in the body.

INCI Name:
(Check PCPC on-line dictionary for latest INCI name)
Butylene Glycol – Water – Sorbitan Laurate – hydroxyethylcellulose – Acetyl Dipeptide-1 Cetyl Ester
No preservatives

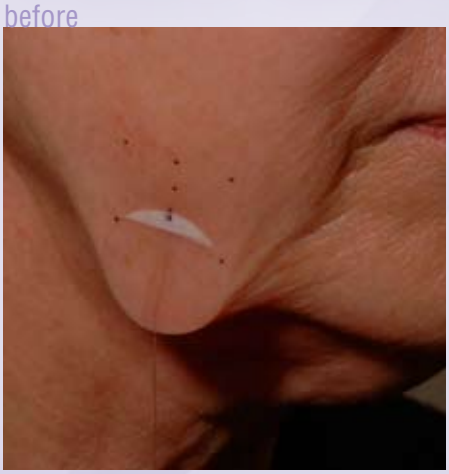
Applications:
Anti-ageing products.

Formulation:
Water soluble.
Introduction into the water phase between 60°C and 80°C.

Recommended use level:
4%

Visible face contour lifting

before



after 1 month

sederma
Member of Croda International Plc
www.sederma.fr
E-mail: sederma@sederma.fr

In vivo tests

26 women with an average age of 62 years (between 54 and 75 years old) applied twice daily on half-face, a day cream containing 4% IDEALIFT™ versus placebo for 2 months.

CUTANEOUS VISCO-ELASTICITY
Aeroflexmeter®

Variation of the skin visco-elastic properties:

Cohesion
- T1 month ..... -2.9 years, p<0.01
- T2 months ..... -4.4 years, p<0.01

Firmness
- T1 month ..... +6.2%/T0, p<0.01, up to +24%/T0
- T2 months ..... +7.8%/T0, p<0.01, up to +28%/T0

Density
- T1 month ..... +10%/T0, p<0.01, up to +32%/T0
- T2 months ..... +9.2%/T0, p<0.01, up to +34%/T0

RESISTANCE TO SAGGING / ANTI-GRAVITY EFFECT
Image analysis

Variation of skin resistance to sagging:
- T1 month ..... +20.5%/T0, p<0.05
- T2 months ..... +24%/T0, p<0.01

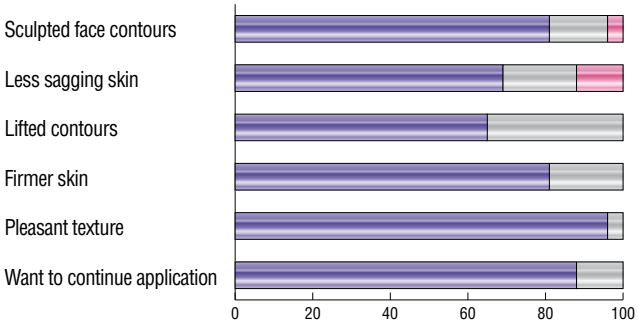
JOWL SURFACE
Image analysis

- T1 month ..... -4.7%/T0, p<0.01, up to -19%/T0
- T2 months ..... -11.3%/T0, p<0.01, up to -21%/T0

JAW LINE SHAPE / CONTOURING EFFECT
FOITS

Variation of jaw line curvature:
- T1 month ..... +5.3%/T0, p<0.05, up to +35%/T0
- T2 months ..... +7.5%/T0, p<0.01, up to +29%/T0

SELF-EVALUATION



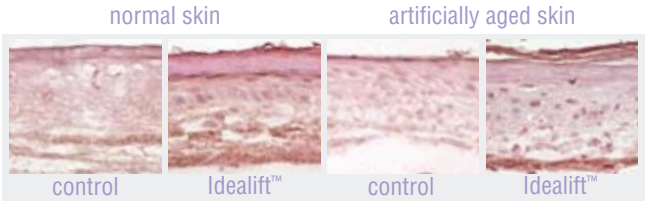
IDEALIFT™ helps ageing skin to fight against cutaneous sagging and decreases the visible effects of gravity on the skin. It promotes a face contour lifting effect perceptible by the consumer after just 1 month.

In vitro tests

Tests performed with 6ppm of Idealift™ peptide.

ELASTIN SYNTHESIS

Elastin/Tropoelastin released :
- Normal human fibroblasts ..... +325%/control, x4.2, p<0.01/control
- Reconstructed skin model ..... +14.6%, p<0.01
- Artificially aged reconstructed skin model ..... +14.8%, p<0.01

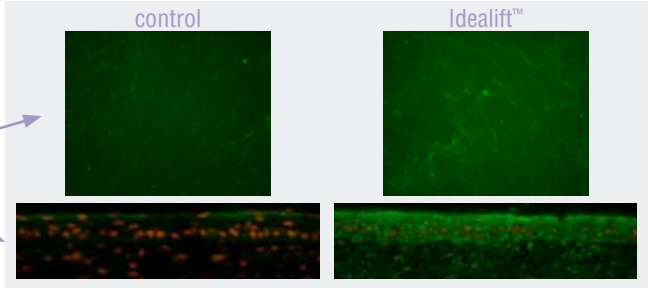


ELASTIN SETTLEMENT

Evaluation of the quantity of elastin/tropoelastin actually settled in the extracellular matrix after release from the fibroblasts: ..... +94%, p<0.01

ELASTIC FIBRE ARCHITECTURE

Evaluation of the synthesis of various molecules necessary for the correct architecture of elastic fibres:
- Fibrillin-1 ..... +747%, p<0.01
- Fibulin-5 ..... +59%, p<0.01
- LOXL-1 ..... +135%, p<0.01
- Transglutaminase ..... +75%, p<0.01
- Decorin ..... +68%, p<0.01



IDEALIFT™ does not only stimulate elastin synthesis but favours a correct and functional elastic fibre architecture by inducing the most important elements involved in tissue structure.

sederma
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