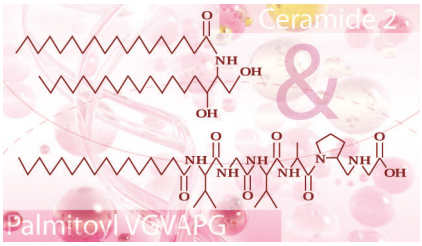
Face Make-up

Patent pending

DERMAXYL®



Ceramide 2 & Pal -VGVAPG

Function:
Anti-aging, wrinkle smoothing and cutaneous barrier repair

Definition:
Association of ceramide 2, the *stratum corneum* cement and the palmitoylated matrikine Pal-Val-Gly-Val-Ala-Pro-Gly

Properties:
Dermaxyl® stimulates cell communication and then repairs the age related skin damage

Characteristics:
Matrikines are messenger peptides specifically involved in repairing damage to the cutaneous matrix,
VGVAPG is the spring fragment of elastin

Points of interest:
Pal-VGVAPG is chemotactic, attracting fibroblasts and monocytes onto the site of matrix repair

Origin:
Synthetic

INCI name:
C12-15 Alkyl Benzoate - Tribehenin - Ceramide 2 - PEG 10 Rapeseed Sterol - Palmitoyl Oligopeptide

Applications:
Skincare and make-up geared to preventing and fighting wrinkles

Formulation:
Oil soluble.
Melt extemporaneously at 85°C and incorporate during the emulsion formation

Recommended use level:
2%

Targeted intervention:

Anti-aging tactics help brush away the footprints of Father Time

sederma

Sederma - member of Croda International Group

CLAIM SUBSTANTIATION

In vitro test: Activation of skin matrix cleansing

Stimulation of the genetic expression of Granulocyte Chemotactic Protein (GCP-2) by DNA array on a 3D keratinocyte model incubated with Pal-VGVAPG. GCP-2 is a chemotactic protein able to recruit cells, involved in the preparation and cleansing of the site, to the damaged area.

Stimulation of GCP-2 expression by Pal-VGVAPG — **227%**

DERMAXYL® BOOSTS THE CELL COMMUNICATION AND DERMAL REPAIR MECHANISMS.

In vivo test: Anti-wrinkle properties

Study performed using 24 female volunteers aged from 42 to 66 years.

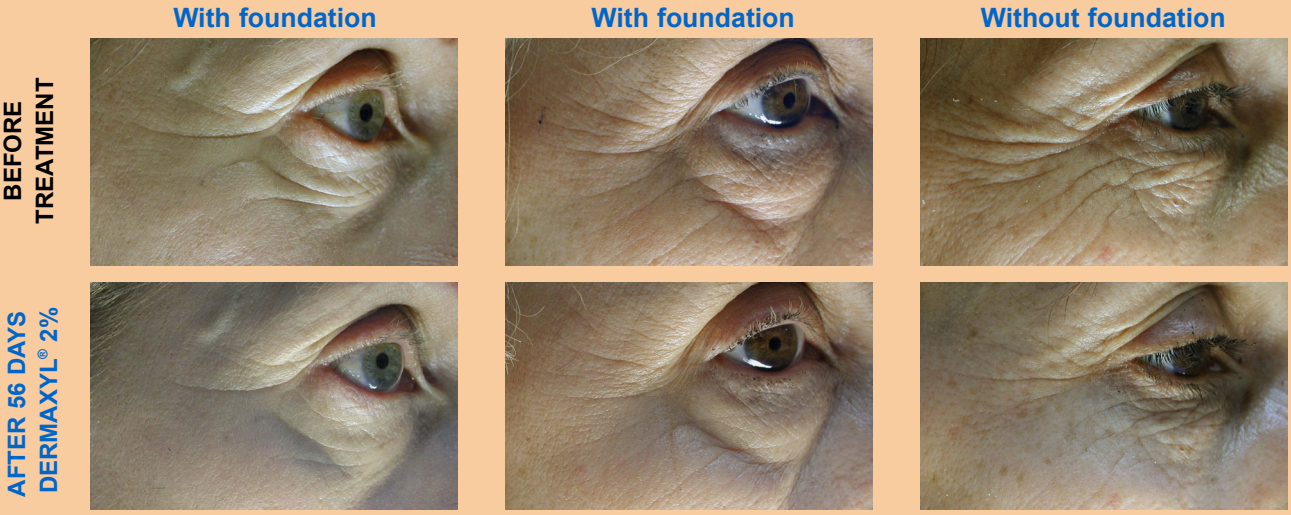
Daily application of a liquid foundation (pigmented or non-pigmented) containing 2% Dermaxyl®, for two months.

Evaluation by image analysis (profilometry).

Since pigments tend to accentuate the appearance of wrinkles, photographs were taken with and without foundation, before and after 56 days of treatment.

Values	Mean	Maximum
Volume of the main wrinkle	-13.7%	-36%
Depth of the main wrinkle	-10.1%	-27%
Surface occupied by deep wrinkles	-40.3%	-98%
Surface occupied by medium wrinkles	-24.5%	-86%

In vivo



Formulation

Anti-aging Emulsion with Dermaxyl®

Suggested formulation ref.: SED0309402A

Part A	%
Water deionized	q.s 100
Ultrez 10 *(Carbomer, Noveon)*	0.25
Part B	**%**
Glycerin	3.50
Preservatives	0.30
Part C	**%**
Volpo-S-10 *(Steareth 10, Croda)*	1.50
Crodafos CS20 Acid *(Cetearyl Alcohol and Ceteth 20 Phosphate and Dicethyl Phosphate, Croda)*	3.50
DC 200 *(Dimethicone, Dow Corning)*	2.00
Crodamol OSU *(Dioctyl Succinate, Croda)*	7.00
Crill 3 (*Sorbitan Stearate, Croda)*	0.40
Part D	**%**
DERMAXYL® *(Sederma)*	2.00
Part E	**%**
Potassium sorbate	0.10
Part F	**%**
Water deionized	4.00
Sodium hydroxide 30%	0.50
Part G	**%**
Fragrance	0.10

Protocol:
Part A: disperse Ultrez 10 in water and let swell for 20 minutes. Heat Part B until disolved then add to Part A. Heat Part (A+B) to 80°C in a bain-marie. Weigh Part C and heat to 80°C in a bain-marie, mixing well. Heat Part D to 85°C and add it extemporaneously to Part C. Add Part (C+D) into Part (A+B) with staro stirring. Then add part E to mixture and homogenize well; allow to cool. At 50°C neutralize with Part F. At 35°C extemporaneously, add Part G.

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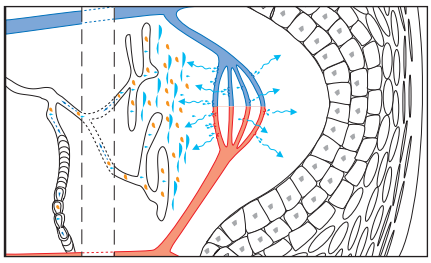
Face

Patent N° WO 03/068141

EYELISS™



Edema formation

Function:
Helps prevent puffiness and reduce bags under the eyes.

Definition:
Combination of 3 active molecules in solution: hesperidin methyl chalcone, dipeptide VW and lipopeptide Pal-GQPR.

Properties:
Hesperidin methyl chalcone: decreases capillary permeability
Dipeptide Valyl-Tryptophane (VW): improves lymphatic circulation.
Lipopeptide Pal-GQPR: improves firmness and elasticity, decreases the inflammatory phenomena.

Characteristics:
A global treatment for puffy eyes based on the association of 3 actives that target specific physiological deficiencies.

INCI name:
(Check CTFA on-line dictionary for latest INCI name)
Aqua (Water) – Glycerin – Hesperidin Methyl Chalcone – Steareth-20 – Dipeptide-2 – Palmitoyl Tetrapeptide-7*
* former INCI name: Palmitoyl Tetrapeptide-3

Applications:
All products (cream, gel, lotion...) intended to reduce of puffy eyes.

Formulation:
Water soluble.
Incorporate at 45°C in emulsions or at room temperature in gels.

Recommended use level:
3%

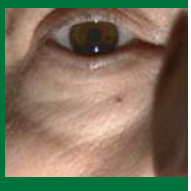
Improvement shown for 70% of volunteers


Before


After


Before


After


Before


After

www.sederma.fr E-mail: sederma@sederma.fr

CLAIM SUBSTANTIATION

March 2006 v.2

In vitro tests

Anti-inflammatory effect of peptide Pal-GQPR

Regulation of UV induced IL6 level produced by keratinocytes

Drainage stimulation of dipeptide VW

Inhibition of Angiotensin Converting Enzyme (ACE)

Ex vivo test

Effect of hesperidin methyl chalcone on capillary permeability

Clinical study

20 female volunteers, aged 40 to 60, with chronic bags under the eyes.

Application of a gel containing 3% EYELISS™ twice a day for 56 days.

3D morphometric measurements by fringe projection at T0, T28 and T56 days.

Morphometric study

Significant results	T28	T56
Mean decrease of bag thickness (in mm)	-0.08	-0.20
Maximum value (in mm)	-0.40	-0.69
Number of volunteers with a reduction in the bag volume	**65%**	**70%**

Self-evaluation

Eye contour smoothing	**62%**
Reduction in the bags	**52%**
Decongestant effect	**52%**

In vitro

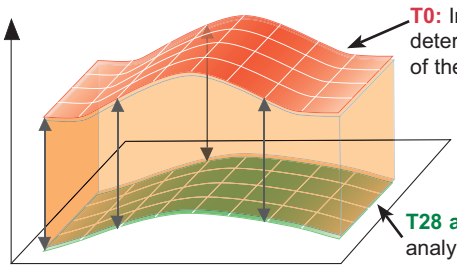
-33% with 3% Eyeliss™

85% with 1% Eyeliss™

Ex vivo

-25% of capillaries' permeability

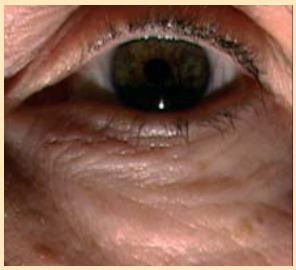
Principle of a 3D morphometric study



The software measures the distance between the surface of the bag before treatment and the surface of the bag after treatment.

In vivo

Before **After**



Formulation

Puffy Eye Gel treatment with EYELISS™

Tested formulation ref.: SED0107234D

Part A	%
Deionized water	qs 100
Ultrez 10 *(Carbomer)*	0.20

Part B	%
Glycerin	5.00
Preservatives	qs

Part C	%
Hydroxyethyl Cellulose	0.20

Part D	%
Pemulen TR2 *(Acrylates / C10-30 Alkyl Acrylate Crosspolymer, Noveon)*	0.20
Crodamol CAP *(Cetearyl Ethylhexanoate, Croda)*	6.00

Part E	%
Potassium sorbate	0.10

Part F	%
Deionized water	4.00
Sodium hydroxide 30%	0.46

Part G	%
EYELISS™ *(Sederma)*	3.00

Part H	
Crillet 1 *(Polysorbate 20, Croda)*	0.50
Fragrance	qs

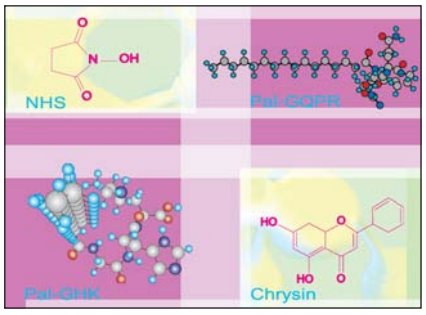
Protocol:

Sprinkle Ultrez 10 in water and allow to swell for 15 minutes. Part B: heat the glycerin to 60°C, dissolve the preservatives. Cool to 40°C. Add Part C to Part B, homogenize, then add Part B+C to Part A with helix stirring. Allow to swell for 1 hour. Add Part D, then Part E to Part (A+B+C), homogenize. Neutralize with Part F. Let swell for 1 hour. Incorporate Part G, homogenize, then add Part H.

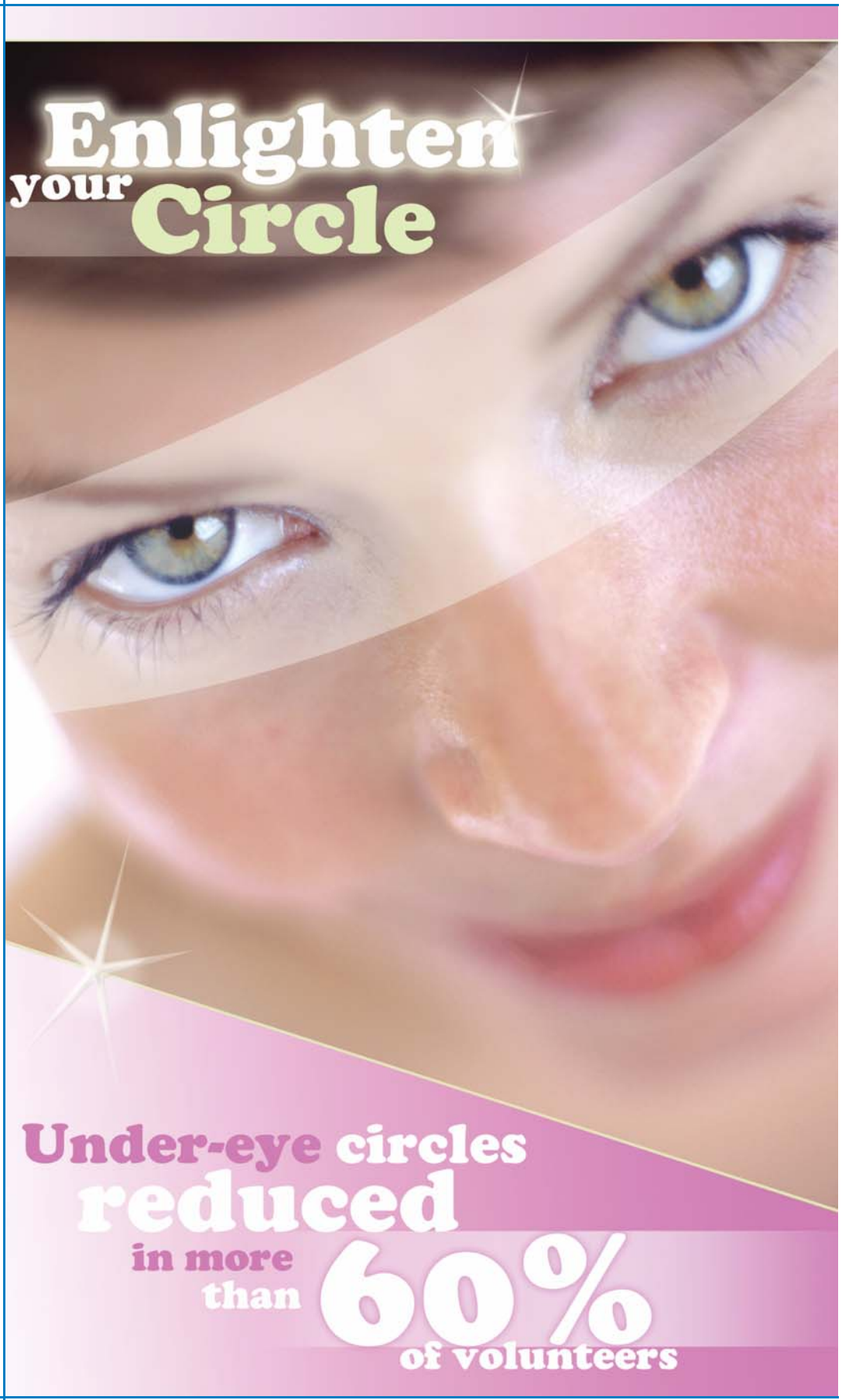
Sederma Inc E-mail: marketing@crodausa.com www.crodausa.com Tel 732-692-1652 Fax 732-417-0804

Patent N° WO 2005/102266

HALOXYL™



Composition of HALOXYL™



Function:
Lessens under eye dark circles.

Definition:
Association of 2 matrikines: Pal-GHK and Pal-GQPR with N-hydroxysuccinimide (NHS) and a flavonoid: chrysin.

Properties:
Pal-GHK and Pal-GQPR reinforce firmness and tone of the eye area. Chrysin and N-hydroxysuccinimide activate the elimination of blood originated pigments responsible for dark circle color and local inflammation.

Characteristics:
Infra-orbital shadows are due to the accumulation of hemoglobin and its colored degradation products (biliverdin, bilirubin and iron) in the dermis and epidermis. Chrysin stimulates the enzyme (UGT_1A_1) leading to the clearance of bilirubin. N-hydroxysuccinimide makes the iron soluble for elimination.

INCI name:
(Check CTFA on-line dictionary for latest INCI name)

Water (Aqua) – Glycerin – Steareth-20 – N-Hydroxysuccinimide – Chrysin – Palmitoyl Oligopeptide – Palmitoyl Tetrapeptide-7*

* former INCI name: Palmitoyl Tetrapeptide-3

Applications:
Dark-circle treatments, eye contour care, concealers.

Formulation:
Water soluble.
Incorporate at 45°C in emulsions or at room temperature in gels.

Recommended use level:
2%

In vitro tests

- **Ability of NHS to bind iron**

  The decrease of color demonstrates the iron complexation by N-hydroxysuccinimide.

- **Anti-inflammatory effect**

  Measurement of the decrease of PGE2 release by keratinocytes and fibroblasts after UVB irradiation, with HALOXYL™.

  HALOXYL™ demonstrates anti-inflammatory properties similar to those of aspirin.

- **Stimulation of expression of UGT**

  Cells in culture are incubated for 3 days with chrysin. The gene expression for UGT_1A_1 is determined by RT-PCR.

  Chrysin strongly stimulates the expression of the enzyme involved in the clearance of bilirubin (end product of hemoglobin degradation).

In vitro

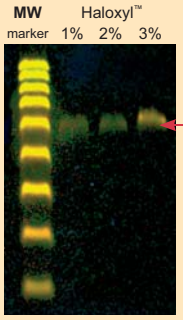
Iron complexation by NHS

N-hydroxysuccinimide binds iron to make it soluble for elimination

Increasing iron complexation by NHS

In vitro

Gene amplification



Product	Gene Amplification
Chrysin 7.8µM (eq. 2% Haloxyl™)	+247%
Chrysin 11.8 µM (eq. 3% Haloxyl™)	+600%

Clinical study: Anti-dark circle efficacy

22 female volunteers applied to the contour of one eye a gel containing 2% HALOXYL™ for 56 days against placebo on the other one. The anti-dark circle effect is assessed by image analysis and measurement of the color parameters (L,a,b system) by a specific software.

	Δa	Δb
Variation	-12.5%*	+10%**
Rate of volunteers with improvement	72%	63%
Variation for volunteers with improvement	**-19.5%**	**+19%**

*significant / T0 (p<0.01) **significant /T0 (p<0.05)

Red and blue colors of dark circles significantly decreased by 19%

Formulation

Anti-Dark Circle Gel with HALOXYL™

Tested formulation ref.: SED0308383 D1t

Part A	%
Deionized water	qs 100
Ultrez 10 *(Carbomer, Noveon)*	0.30
Part B	**%**
Glycerin	5.00
Preservatives	qs
Part C	**%**
Hydroxyethyl Cellulose	0.30
Part D	**%**
Pemulen TR2 *(Acrylates / C10-30 Alkyl Acrylate Crosspolymer, Noveon)*	0.20
Crodamol CAP *(Cetearyl Ethylhexanoate, Croda)*	6.00
Part E	**%**
Potassium sorbate	0.10
Part F	**%**
Deionized water	4.00
Sodium hydroxide 30%	0.46
Part G	**%**
Crillet 1 (Polysorbate 20, Croda)	0.50
Part H	**%**
HALOXYL™ (Sederma)	2.00

Protocol

Part A: Sprinkle Ultrez 10 in water and allow to swell for 15 minutes. Part B: heat the glycerin to 60°C, dissolve the preservatives. Cool to 40°C. Add Part C to Part B, homogenize, then add Part B+C to Part A with helix stirring. Allow to swell for 1 hour. Add Part D, then Part E to Part (A+B+C), homogenize. Neutralize with Part F. Let swell for 1 hour. Incorporate Part G, homogenize, then add Part H.

Non-warranty:
This formulation has been subjected to limited stability tests and has been shown to perform well. However formulators adopting this approach should ensure to their own satisfaction long term stability and functionality. It is good practice to conduct safety tests on all final formulations prior to marketing. Suggested uses should not be taken as an inducement to infringe any existing patents.

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BARNET

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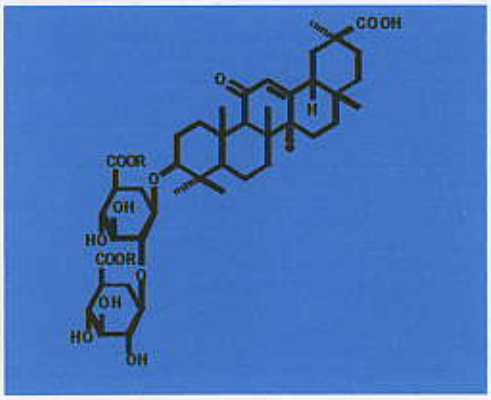
NET-DG

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***