

Vascular tonicity enhancement and inhibition of rosacea

Into the skin, when microcirculation undergoes vasodilation some cutaneous dysfunctions can appear such as rosacea, oedema, micro-inflammations... **Rosacea** characteristically involves the central region of the face, causing persistent redness or transient flushing over the areas of the face and nose that normally blush: mainly the forehead, the chin, and the lower half of the nose. The major symptoms include red or pink patches, visible tiny broken or dilated small blood vessels, oedema, micro-inflammations, small red bumps, red cysts and pink or irritated eyes.

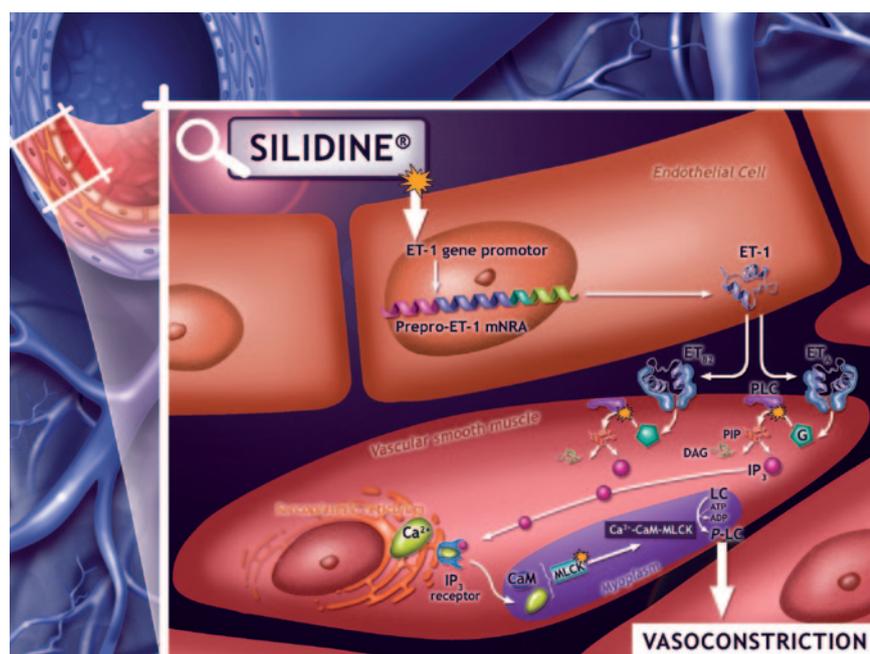
Also, **heavy legs syndrome** is often one of the first signs telling of the venous insufficiency. The dilation of the blood microvessels at the level of the lower limbs induces a dysfunction of the venous return and a stagnation of the blood in the bottom of legs. Thus, when blood stays for too long in the lower limbs, people feel pain, pins and needles, pinching and itchiness.

In order to counteract these phenomenons, an **uncommon marine active SILIDINE®** has been developed by metabolic induction of the microalga *Porphyridium cruentum*. SILIDINE® is a subtle mix between small oligosaccharides and essential oligoelements, **to correct the heavy legs syndrome, and cutaneous dysfunctions as rosacea in sensitive skin care.**

BIOLOGICAL MECHANISM

The use of SILIDINE® induces the stimulation of the synthesis of endothelin-1 (ET-1) by endothelial cells (and fibroblasts) at the level of veins and capillaries. The binding of ET-1 to the surface receptors (ET_A and ET_{B2} receptors) of vascular smooth muscle cells induces a signal that spreads from the outside to the inside of the plasma membrane and activates several effectors that ultimately initiate vasoconstriction:

- ▶ The activated receptors interact with a G-protein that in turn activates phospholipase C (PLC).
- ▶ The activated PLC induces hydrolysis of phosphatidyl inositol (PIP) and formation of inositol 1,4,5-triphosphate (IP₃) and 1,2-diaclyglycerol (DAG).
- ▶ IP₃ binds to its receptor on the surface of sarcoplasmic reticulum, this opens Ca²⁺ channels and Ca²⁺ from sarcoplasmic reticulum is entering the myoplasm.
- ▶ Ca²⁺ combines with calmodulin and this complex activates the enzyme myosin light chain kinase (MLCK), which in turn phosphorylates myosine light chain (LC).
- ▶ The phosphorylated myosin filament (P-LC) combines with the actin filament.
- ▶ Finally the smooth muscle contracts inducing a constriction of the vasculature.



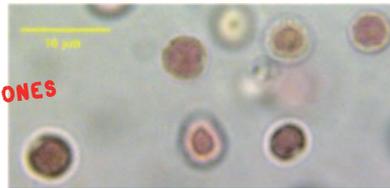
ET-1: endothelin-1 ;
 ET_A: endothelin receptor, subtype A ; ET_{B2}: endothelin receptor, subtype B2 ;
 G: G-protein ;
 PLC: phospholipase C ; PIP: phosphatidyl inositol ;
 DAG: 1,2-diaclyglycerol ;
 IP₃: inositol 1,4,5 - trisphosphate ;
 CaM: calmodulin ;
 MLCK: myosin light chain kinase ;
 LC: myosin light chain ;
 P-LC: phosphorylated myosin light chain.

- **INCI NAME (suggested):** Water, Porphyridium Cruentum Exsuded Culture Medium
- **PRESERVATIVE:** Citric Acid, Sodium Benzoate, Potassium Sorbate

PRODUCTION: THE METABOLIC INDUCTION

SILIDINE® is made from the red microalgae *Porphyridium cruentum* by metabolic induction.

NO GMO
NO SYNTHETIC HORMONES

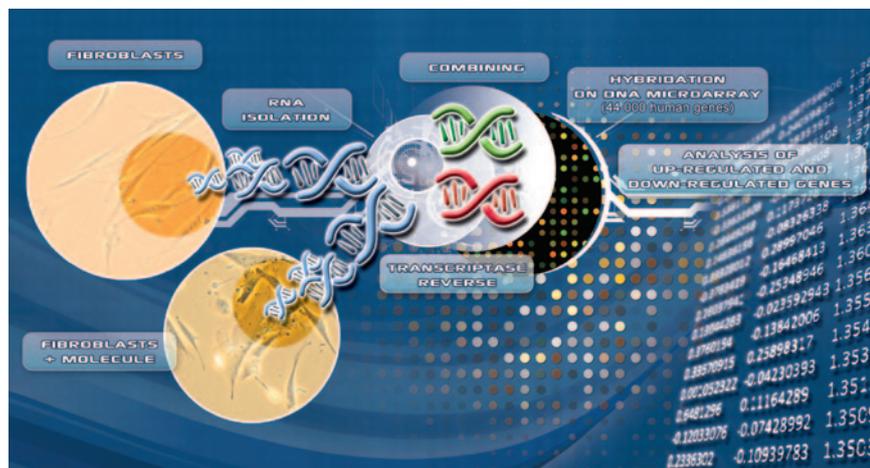


The culture of *Porphyridium cruentum* is submitted to an oxidative stress resulting from photosynthesis oxygen level increase in the culture medium. Facing this oxidative stress, *Porphyridium cruentum* adapts itself to environmental changes, reacts and synthesises different molecules like oligosaccharides and modifies the oligoelements environment.

Oligoelement composition of SILIDINE®:

Aluminium	Al
Calcium	Ca
Chloride	Cl
Iron	Fe
Potassium	K
Magnesium	Mg
Manganese	Mn
Sodium	Na
Phosphorus	P
Sulphur	S
Titanium	Ti

PREDICTIVE TEST: Transcriptomic analysis with DNA microarray

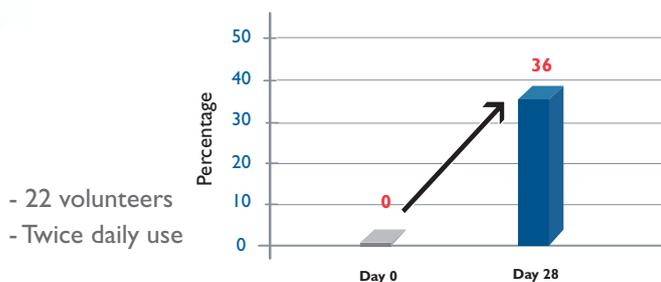


SILIDINE® stimulates the expression of the endothelin-1 gene, responsible of the vascular smooth muscle contraction.

EFFICACY

INVIVO TEST - EFFECT ON HEAVY LEG SYNDROME
Clinical evaluation: SILIDINE® 1% (powder form) -28 days

% of volunteers with variation of the cutaneous microcirculation



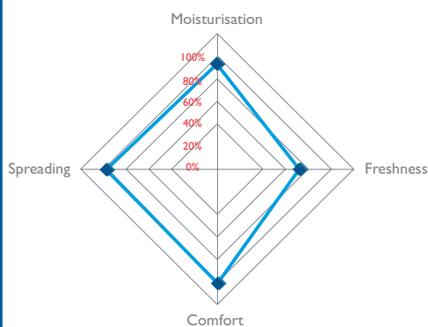
Measurement of the Doppler effect has shown that SILIDINE® allows a variation in the cutaneous microcirculation for 36% of volunteers.

SILIDINE® improves the vascular tonicity and helps to decrease the heavy leg syndrome.

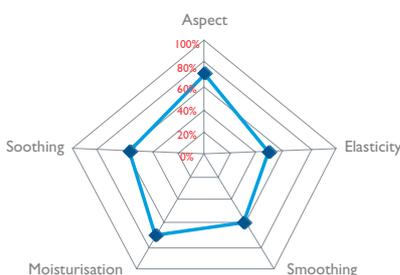
IN VIVO TEST - EFFECT ON HEAVY LEG SYNDROME

Sensory test: SILIDINE® 1% (powder form) - 28 days

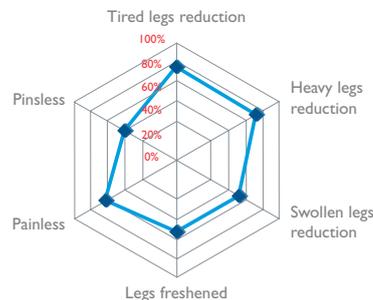
Global auto-evaluation immediately after application



Efficacy on skin properties



Efficacy on legs sensations



More than 70% of volunteers felt improvement on: tired legs sensation and heavy legs effect.

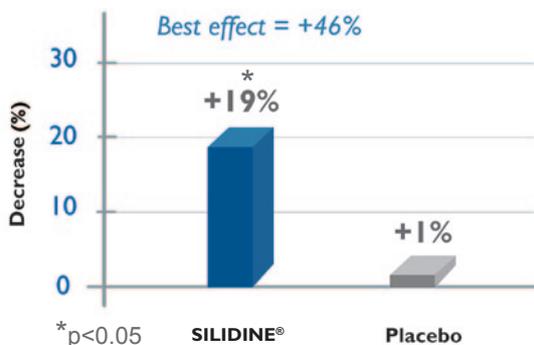
Auto-evaluation test results show a positive effect of SILIDINE® at 1% regarding the global properties of the skin and also the specific sensations of the heavy legs.

SILIDINE® improves the aspect of the skin and helps to decrease the heavy legs syndrome.

IN VIVO TEST - EFFECT ON REDNESS AND ROSACEA

Clinical test: SILIDINE® 3% (liquid form) - 28 days

Face redness reduction



*p<0.05

- Double blind
- 14 volunteers
- Twice daily use

SILIDINE®

Volunteer 14: day 0



Decrease of 26%

day 28



PLACEBO

Volunteer 14: day 0



Decrease of 6%

day 28



SILIDINE® significantly decreases the red colour on the skin face of the volunteers by 19%. This reduction appeared on 86% of volunteers.

SILIDINE® improves the vascular tonicity and helps to decrease the effects of rosacea as redness.

SILIDINE®:

- Stimulates the expression of the gene of endothelin-I and the synthesis of the protein by fibroblasts and endothelial cells
- Enhances the binding of endothelin-I to the surface receptors (ET_A and ET_{B2}) of smooth muscle cells
- Involves a signal that spreads from the outside to the inside of the plasma membrane and activates several effectors that initiate the release of Ca²⁺, the formation of the complex Ca²⁺ - calmodulin - myosin light chain kinase, and the phosphorylation of the myosin light chain
- Induces the constriction of the vasculature



The vascular tonicity is improved

EFFECTS OF COSMETIC APPLICATION

- Vasoconstriction of veins and cutaneous microvessels
- Correction of cutaneous dysfunctions (rosacea, inflammation, dark eye circles, oedema, ...)
- Reduction of heavy legs syndrome
- Regeneration of cells skin
- Promotion of skin aspect

COSMETIC USES

- ✓ Vascular tonicity enhancement care
- ✓ Body tonicity skin care
- ✓ Sensitive skin care

FORMULATIONS

- **USE LEVEL**
1 to 5 %
- **pH LEVEL**
4.0 - 10.0
- **CAUTION FOR USE**
- Add at the end of preparation, when at 35-40°C for emulsions, while cooling.

TECHNICAL DATA

CHARACTERISTICS

Organoleptic: Appearance: Liquid
Colour: Pale yellow to yellow
Odour: Characteristic

Solubility: Water: Soluble (10%)
Ethanol: Insoluble (10%)

pH: 3.4 - 4.0
(It is possible to buffer if needed)

TOLERANCE TESTS

Eye irritation: Non irritant
Skin irritation: Non irritant
Mutagenicity: Non mutagenic
Phototoxicity: None
Sensitization: Hypoallergenic

STORAGE

Store protected from light in their original packaging and at room temperature (15-25°C).

Warning: The company cannot assume any liability or risk involved in the use of its products since the conditions of use are beyond our control. We assume no responsibility concerning the formulations which are brought to the market and which contain one or several of our products. It is incumbent to the formulators to take all necessary precautions and, in particular, to comply with all required legal and regulatory steps and formalities.

All results described into this document represent the most relevant data.

