



## Clinical Studies from:

- Eyeless
- Lipotec
- Matrixyl
- PhytoCell
- BV-OSC
- SYN-EYE



# Clinical Studies

Eyeless

## FIGHT AGAINST BAGS UNDER THE EYES

### Function and Characteristics:

EYELISS is a combination of 3 active molecules in solution:

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

### Cosmetic interest (properties):

Tiredness, hypertension or the intake of certain medicines, in addition to the natural effects of ageing, contribute to the formation of bags under the eyes.

EYELISS helps to prevent and fight bags under eyes as well as smoothing the appearance of fine lines by firming and toning the skin.

### Applications:

All products (creams, gels, lotions...) intended for the treatment of puffy eyes.

Recommended use level: 3%

### CTFA / INCI name:

Water (Aqua) - Glycerin - Hesperidin Methyl Chalcone - Steareth-20 - Dipeptide-2 - Palmitoyl Tetrapeptide-3

### Specifications:

Appearance	: clear liquid
Colour	: brown
Odour	: characteristic
pH	: 6.0 – 7.0
Density $d_{20}^{20}$	: 1.050 – 1.070
Refractive index (at 25°C)	: 1.360 – 1.380
Water content (K. Fischer)	: 72 – 82%
Val-Trp-OH content	: 0.08 – 0.12%
Hesperidine content	: 4 – 6%
Pal-GQPR content	: 0.025 – 0.035%
Bacteria	: < 100 germs/g
Yeast and moulds	: < 10 germs/g

Sederma patents: FR 2 836 042 - WO 03/068141 - EP 03 718 861.2 - JP 2002.207075

## CLAIM SUBSTANTIATION

### IN VITRO

#### Anti-inflammatory effect of lipopeptide Pal-GQPR with 3% EYELISS:

- Regulation of UV induced IL6 level produced by keratinocytes : **33%**

#### Drainage stimulation of dipeptide VW with 1% EYELISS:

- Inhibition of Angiotensin Converting Enzyme (ACE) : **85%**

### EX VIVO

#### Effect of hesperidin methyl chalone (HMC) on capillary permeability:

- Decrease of capillaries' permeability : **25%**

### Clinical study:

20 female volunteers, aged between 40 and 60 presenting chronics bags under the eyes / Twice daily application for 56 days of a gel containing 3% EYELISS.

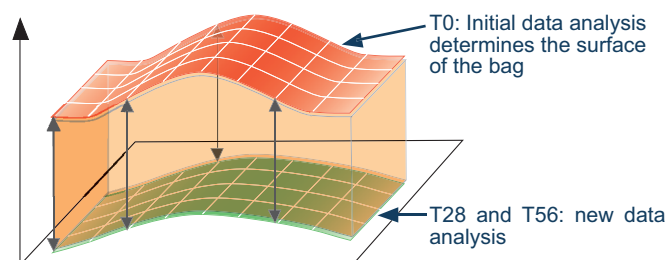
### Morphometric study:

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

### Self-evaluation:

- Eye contour smoothing : **62%**  
 - Reduction of the bags : **52%**  
 - Decongestant effect : **52%**

### 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

### Before



### After





# Clinical Studies

Lipotec



## PROPERTIES AND APPLICATIONS

- The draining effect of EYESERYL<sup>®</sup> achieves a reduction of puffy eyebags in only 15 days – fast anti-eyebag action

EYESERYL<sup>®</sup> can be incorporated in cosmetic formulations such as emulsions, gels, sera, etc., where a reduction of puffiness under the eyes is desired.

## TECHNICAL INFORMATION

### PRODUCT SPECIFICATIONS

Code:	PD070
Appearance:	Transparent Solution
INCI name:	Water, Acetyl Tetrapeptide-5
Active ingredient content:	0.1% Acetyl Tetrapeptide-5
Solvent:	Demineralised water
Preservative:	0.5 % Phenonip

### PROCESSING AND DOSAGE

EYESERYL<sup>®</sup> is presented as **EYESERYL<sup>®</sup> Solution**, an aqueous solution containing 1 g/L of the powder. It can be incorporated at the final stage of the manufacturing product, provided the temperature is below 40 °C. Taking into consideration the concentration of peptide in **EYESERYL<sup>®</sup> Solution**, it is recommended that 3 to 10% of the solution is present in the final formulation in order to obtain significant eyebag-reducing activity.

### STORAGE AND SHELF LIFE

Keep in a clean, cool and dark place. If the product is stored as recommended it will remain stable for at least 12 months.

### SAFETY

EYESERYL<sup>®</sup> has been tested in vitro for ocular irritation and is non irritant at the concentration of use. All the raw materials involved in the formulation are regarded as safe at the concentrations of use.



Results

The ACE inhibitory activity of EYESERYL<sup>®</sup> is shown in Fig. 1. EYESERYL<sup>®</sup> inhibited ACE activity at all tested concentrations, and the effects were dose dependent.

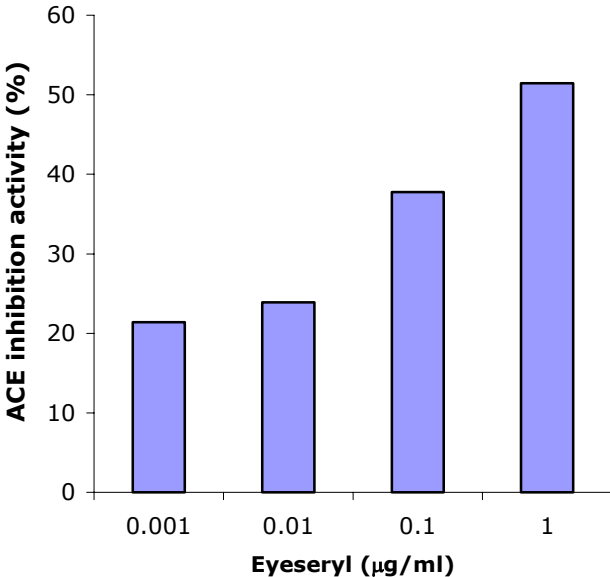


Figure 1. ACE inhibitory activity of EYESERYL<sup>®</sup>



## IN VIVO

EYESERYL<sup>®</sup> has been tested in vivo on a group of 20 female volunteers. A cream containing 0.01% EYESERYL was applied twice a day during 60 days. Pictures were taken at 0, 15, 30, 45 and 60 days.

A dermatologist assigned a score to the decrease in eyebag puffiness:

- 1 – no reduction,
- 2 – slight reduction,
- 3 – fairly good reduction,
- 4 – good reduction

Volunteer A



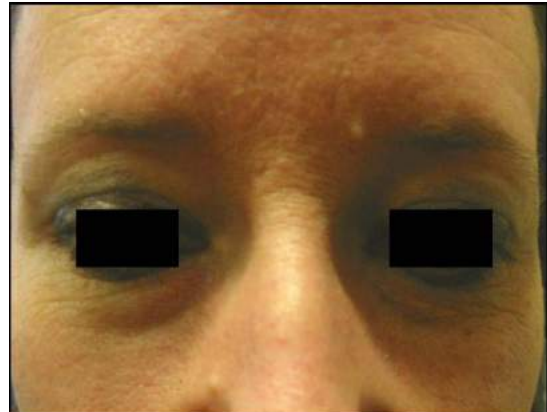
Day 0



Day 15

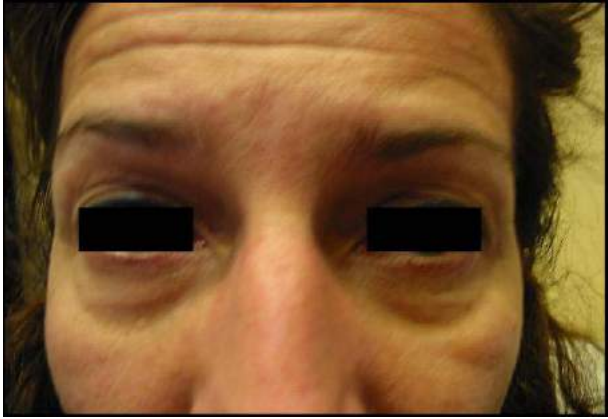


Day 30



Day 45

Voluntaria B



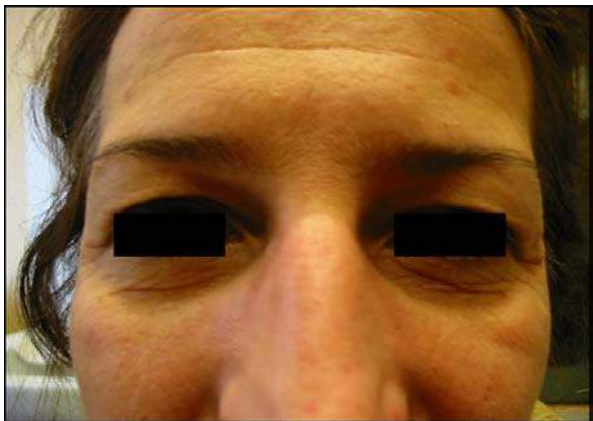
Day 0



Day 15

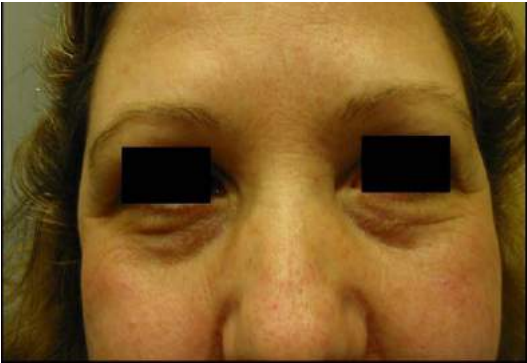


Day 30

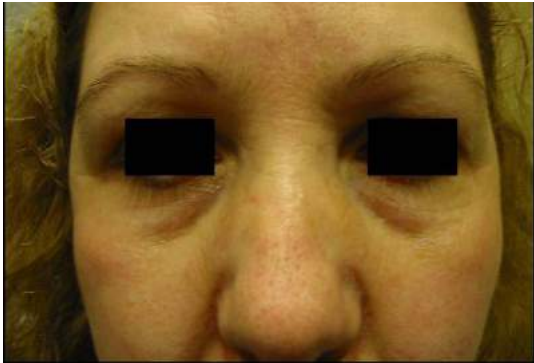


Day 45

Voluntaria C



Day 0



Day 15



Day 30



Day 45

## **Conclusions**

Puffiness under the eyes is greatly reduced, even after only 15 days! - 70% of the volunteers had improved at Day 15.

At the end of the test, 95% of the volunteers had improved:

- ✓ 30% showed a slight improvement (grade 2)
- ✓ 30% showed a fairly good improvement (grade 3)
- ✓ 35% showed a good improvement (grade 4)

## GENERAL PRODUCT INFORMATION

<b>Trade name</b>	EYESERYL <sup>®</sup>
<b>Product code</b>	PD070

## INGREDIENTS

<b>INCI name</b>	<b>CAS No</b>	<b>EINECS No</b>
WATER (AQUA)	7732-18-5	231-791-2
ACETYL TETRAPEPTIDE-5	N.L.	N.L.
PHENOXYETHANOL	122-99-6	204-589-7
METHYLPARABEN	99-76-3	202-785-7
BUTYLPARABEN	94-26-8	202-318-7
ETHYLPARABEN	120-47-8	204-399-4
PROPYLPARABEN	94-13-3	202-307-7
ISOBUTYLPARABEN	4247-02-3	224-208-8

<sup>a</sup> Not Listed



# Clinical Studies

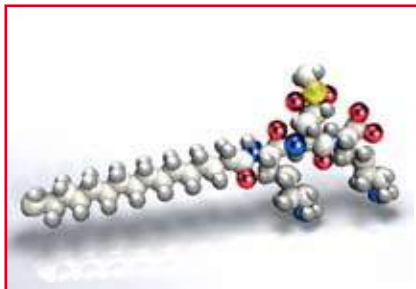
Matrixyl





# MATRIXYL<sup>®</sup> synthe'6<sup>™</sup>

Patent WO 2010/082175



Palmitoyl-KMO<sub>2</sub>K

**Function:**

Wrinkle filler.

**Definition:**

A dioxygenated lipopeptide Palmitoyl-Lysyl-Dioxymethionyl-Lysine.

**Properties:**

Evens out skin relief and smoothes wrinkles from the inside by rebuilding the skin where it is needed, particularly on the forehead and crow's feet.

**Characteristics:**

Matrikine-like effect that stimulates the synthesis of 6 major constituents of the skin matrix and dermal-epidermal junction (collagen I, III, IV, fibronectin, hyaluronic acid and laminin 5).

**Points of interest:**

MATRIXYL<sup>®</sup> synthe'6<sup>™</sup> is derived from the tripeptide KMK naturally found in collagen VI and laminins.

**INCI Name:**

(Check PCPC on-line dictionary for latest INCI name)

Glycerin – Water (Aqua) – Hydroxypropyl Cyclodextrin – Palmitoyl Tripeptide-38

**Applications:**

Skincare and make-up designed to fight wrinkles.

**Formulation:**

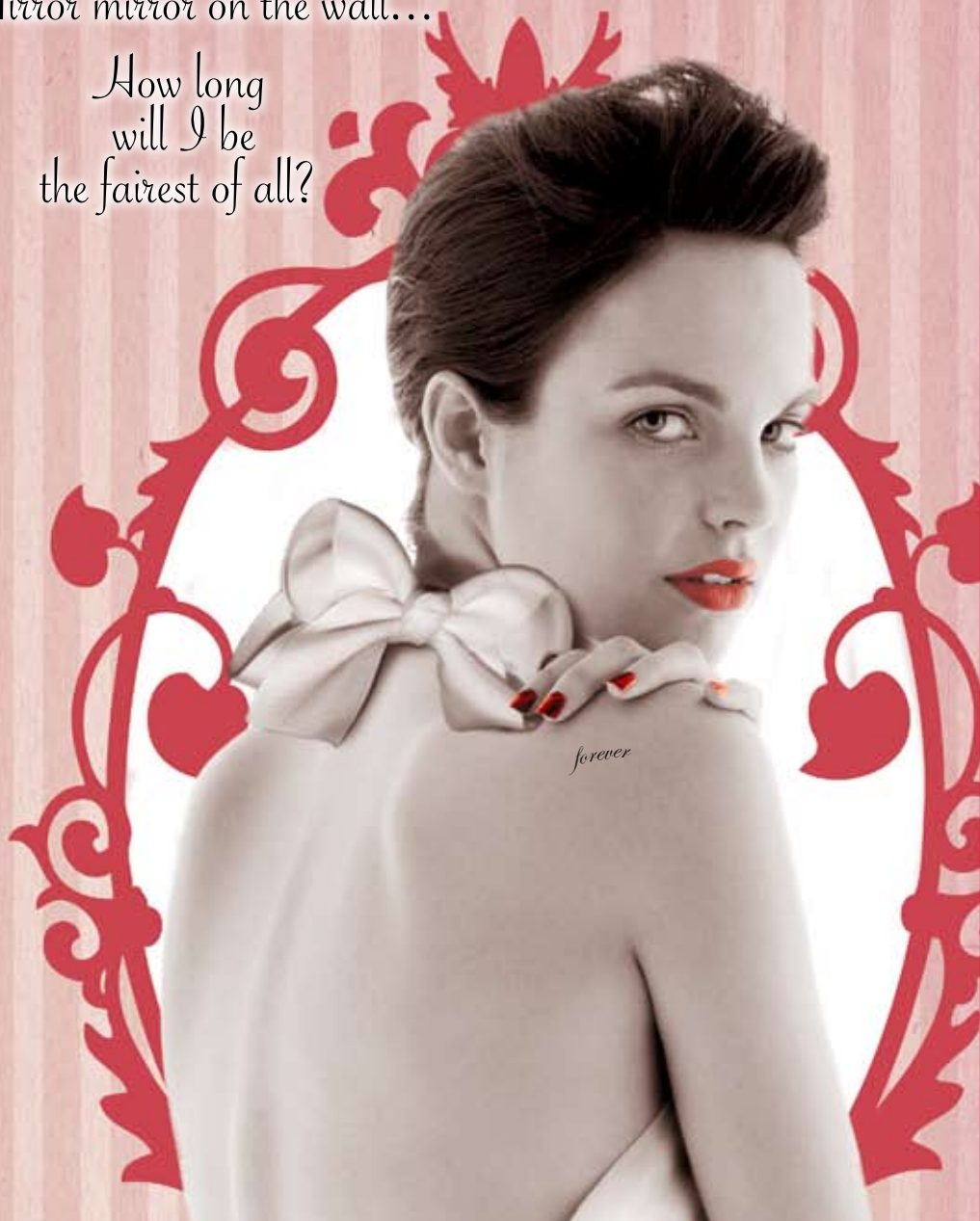
Water soluble. Add to the emulsion between 25°C and 80°C.

**Recommended use level:**

2%

Mirror mirror on the wall...

How long will I be the fairest of all?



**matrixyl inside**

**6 A powerful peptide that boosts skin-rebuilding essentials**

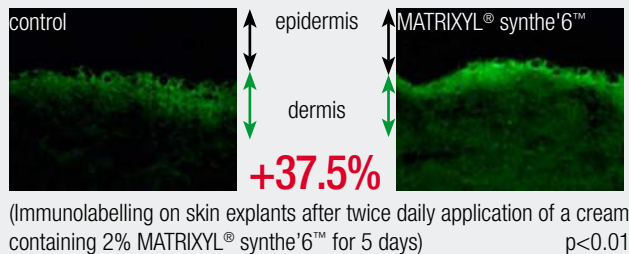
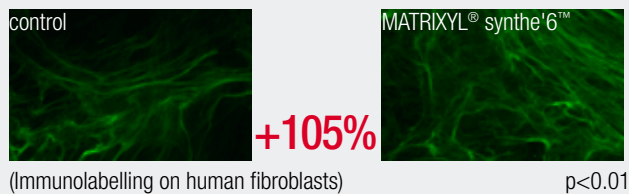
BEFORE      AFTER 2 MONTHS

**3-Dimensional decrease in wrinkles by 31% up to 100%**

## SYNTHESIS OF 6 MAJOR CONSTITUENTS OF THE SKIN

### ● COLLAGEN I, III, IV & HSP47

#### ● COLLAGEN I



### ● HYALURONIC ACID

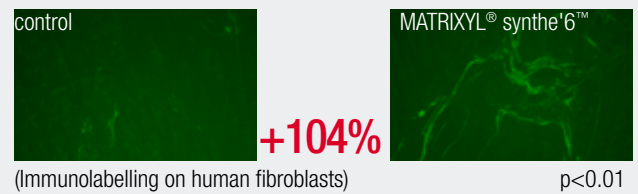
● Hyaluronic acid ..... **+174%**,  $p < 0.01$   
(ELISA method on human keratinocytes)

### ● FIBRONECTIN

● Fibronectin ..... **+59%**,  $p < 0.01$   
(ELISA method on human fibroblasts)

Tests performed with 2% MATRIXYL® synthe'6™.

#### ● COLLAGEN III



● COLLAGEN IV ..... **+42%**,  $p < 0.01$   
(ELISA method on human fibroblasts)

● HSP47 ..... **+123%**,  $p < 0.01$   
(Western blot on human fibroblasts)  
Chaperone protein HSP47 is one of the components necessary for the maturation of collagens I to V.

### ● LAMININ-5



● Laminin-5 ..... **+75%**,  $p < 0.01$   
(ELISA method on human keratinocytes)

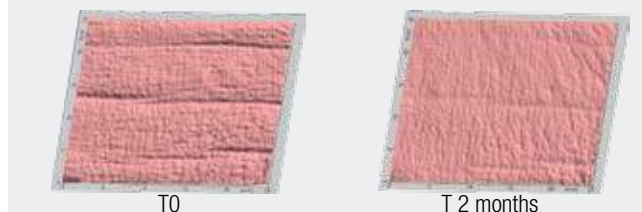
**MATRIXYL® synthe'6™ significantly increases the synthesis of 6 major constituents of the matrix and dermal-epidermal junction.**

## ANTI-WRINKLE EFFICACY

25 female volunteers aged from 42 to 70 years old with forehead lines and crow's feet. Twice daily application of a cream containing 2% MATRIXYL® synthe'6™ for 2 months vs placebo.

### ● ON THE FOREHEAD - FOITS

● Lifting effect ..... **+28%/T0**,  $p < 0.05$ , up to **+77%**  
● Wrinkle volume ..... **-31%/T0**,  $p = 0.055$ , up to **-100%**  
● Maximum wrinkle depth ..... **-16.3%/T0**,  $p < 0.05$  up to **-62%**



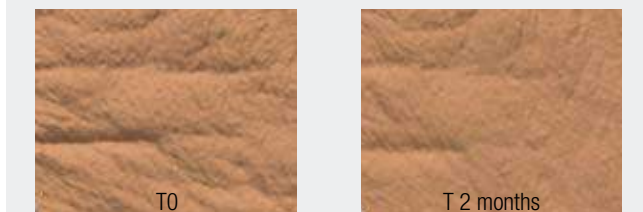
### ● ON THE CROW'S FEET

#### FOITS

● Lifting effect ..... **+12.6%/placebo**,  $p < 0.05$   
● Wrinkle volume ..... **-21.1%/placebo**,  $p < 0.05$

#### SILFLO® (n=24 volunteers)

● Surface occupied by deep wrinkles (>100 µm) ..... **-28.5%/placebo**,  $p < 0.05$   
● Main wrinkle average depth ..... **-15%/placebo**,  $p < 0.05$   
● Wrinkle spread (angle) ..... **+8.4%/placebo**,  $p < 0.05$



**MATRIXYL® synthe'6™ rebuilds the skin network that keeps the skin smooth.  
After 2 months, the forehead and crow's feet wrinkles are evened out just like a facelift.**

## Formulation

## Wrinkle Smoothing Intervention gel-cream

formula Ref.: SED1003840 C

<b>Part A</b> .....%	<b>Part D</b> .....%	<b>Part H</b> .....%
Water deionized	Optasense G82 (Acrylic Acid / Alkylmethacrylate Copolymer)	Perfume (Azalea, Expressions Parfumées)
Optasense G83 (Carbomer, Croda)	DC 200 5 cps (Dimethicone, Dow Corning)	0.20
<b>Part B</b> .....%	<b>Part E</b> .....%	<b>Protocol:</b>
Crillet 1 (Polysorbate 20, Croda)	Potassium Sorbate	Part A: sprinkle the carbomer into water and allow swelling for 30 minutes without stirring. Weigh and mix Part B. Weigh and mix Part C. Add Part C to Part A and mix. Weigh and mix Part D. Pour Part B and Part D into Part A+C with helix stirring (s= 500 rpm). Extemporaneously, add Part E to Part A+B+C+D; homogenize well during 1 hour. Neutralize with Part F and homogenize well. Add Part G and homogenize well. Add Part H and homogenize well.
Crodamol GTCC (Caprylic/Capric Triglyceride, Croda)	<b>Part F</b> .....%	
Cromollient DP3A (Di-PPG-3 Myristyl Ether Adipate, Croda)	Water deionized	
<b>Part C</b> .....%	Sodium hydroxide 30%	
Butylene Glycol	<b>Part G</b> .....%	
Preservatives	<b>MATRIXYL® synthe'6™ (Sederma)</b>	
		2.00

**Non-warranty:** This formulation has been subject 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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# Clinical Studies

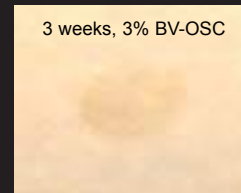
BV-OSC



Barnet Products Corporation 140 Sylvan Avenue Englewood Cliffs NJ 07632  
Tel 201 346 4620 Fax 201 346 4333 Web barnetproducts.com

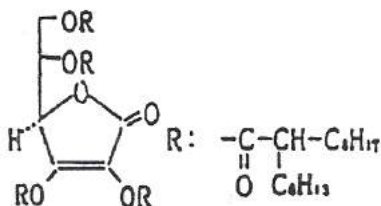
## BV-OSC

- Whitening - now tested *in vivo*
- MMP Inhibitor
- Anti-Oxidant
- Collagen Synthesis & Protection
- DNA Protection



### DESCRIPTION

BV-OSC (Tetrahexyldecyl Ascorbate) is a stable, oil soluble form of Vitamin C.



### PROPERTIES

- \* BV-OSC at 0.1% reduces melanin synthesis by 80%.
- \* BV-OSC at 3% *in vivo* reduces Delta-L value by 15% vs. placebo (22 people), a way to measure whitening effect
- \* BV-OSC at 0.1% *in vitro* increases collagen by 50%.
- \* BV-OSC at 10% *in vivo* treats acne with 80% of patients (12 people)
- \* BV-OSC increases collagen synthesis at least twice as much as ascorbic acid.
- \* BV-OSC inhibits MMP-2 and MMP-9 over 3 times better than ascorbic acid.
- \* BV-OSC penetrates the skin 4 times better than Magnesium Ascorbyl Phosphate.
- \* BV-OSC delivers pure Vitamin C 50 times better than ascorbic acid.
- \* BV-OSC decreases 8-OHdG induced by UV-A.
- \* BV-OSC decreases p53 expression induced by UV-B.
- \* BV-OSC protects the cells against UV-B better than other esters of Vitamin C.

### FORMULATION

BV-OSC is a slight to pale yellow liquid with a faint characteristic odor. It is very soluble in ethanol, hydrocarbons, esters and vegetable oils. It is insoluble in glycerin and butylene glycol. BV-OSC should be added into the oil phase at temperatures below 80°C. It can be used in formulas with a pH range of 3 to 6. BV-OSC can also be used at pH 7 in combination with chelating agents or antioxidants (guidelines are offered). Use level is 0.5% - 3%. BV-OSC is approved as a quasi-drug in Korea at 2%, and in Japan at 3%.

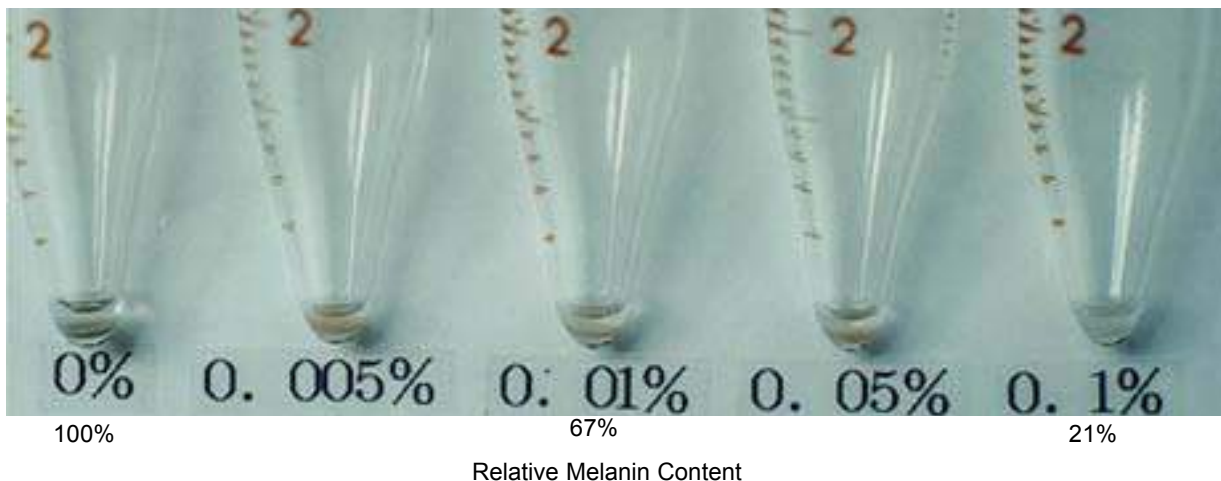
### LEGISLATION

INCI Name: Tetrahexyldecyl Ascorbate      JSCI: 532297 (Ascorbyl Tetra 2-Hexyldecanoate)  
CAS: 183476-82-6      EINECS:

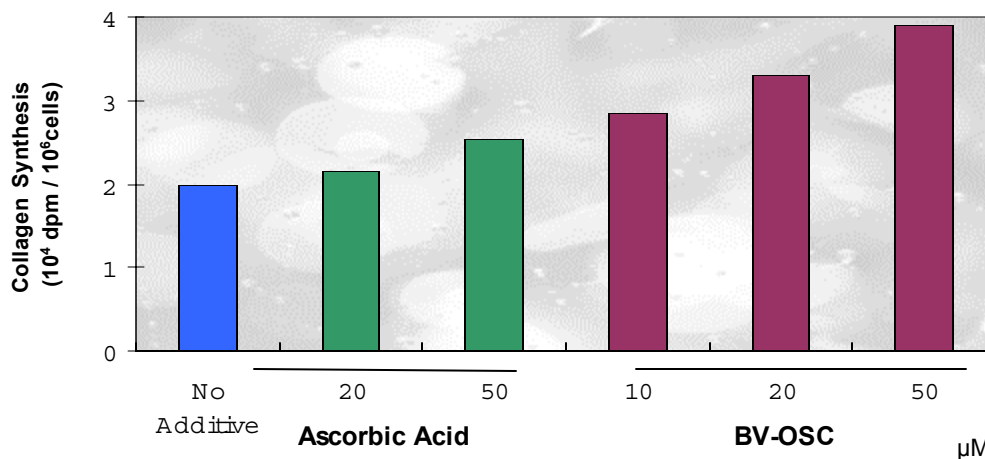
KOREA: Approved as a functional ingredient for whitening at 2%.

# BV-OSC

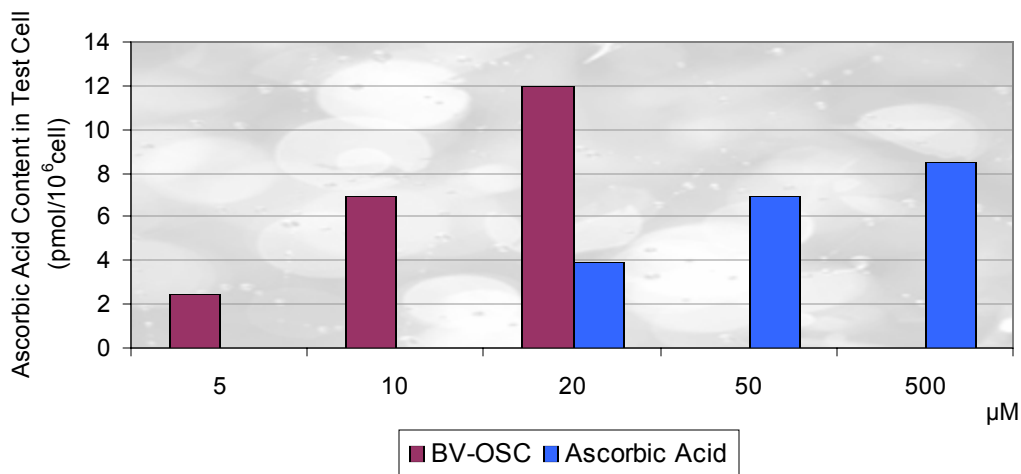
## REDUCTION OF MELANIN SYNTHESIS



## COMPARISON OF ABILITY FOR COLLAGEN SYNTHESIS



## UPTAKEN CONTENT OF INTRACELLULAR (KERATINOCYTES) ASCORBIC ACID



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# BV-OSC

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## ADDITIONAL FORMULATING GUIDELINES

The following information should be considered when formulating with BV-OSC.

1. pH must be below 6.0 (for the water phase): Although BV-OSC is oil soluble, it's stability can be effected by the pH. The factory suggests that the pH be adjusted to below 6.0 before BV-OSC is added to the formulation. (adjusting it after it is added may be too late).
2. Use of chelating agents and antioxidants (tocopherol) is suggested.
3. Avoid long exposure of the formulation to strong heat.
4. BV-OSC should not be added alone in to water. It should be mixed with at least an equal amount (3.5%) of non-polar oils (squalane or esters)
5. Quasi Drug whitening formulation must contain 3% BV-OSC. The specified range is + 10%, which calculates to 2.7 - 3.3%.
6. BV-OSC in the formulation. The factory therefore suggests that 3.3% BV-OSC should be added to the finished formulation to insure compliance with the required range of 2.7 - 3.3%.
7. The use of Hectorites with BV-OSC may cause instability. Customer should evaluate the stability upon the use of BV-OSC and Hectorites.





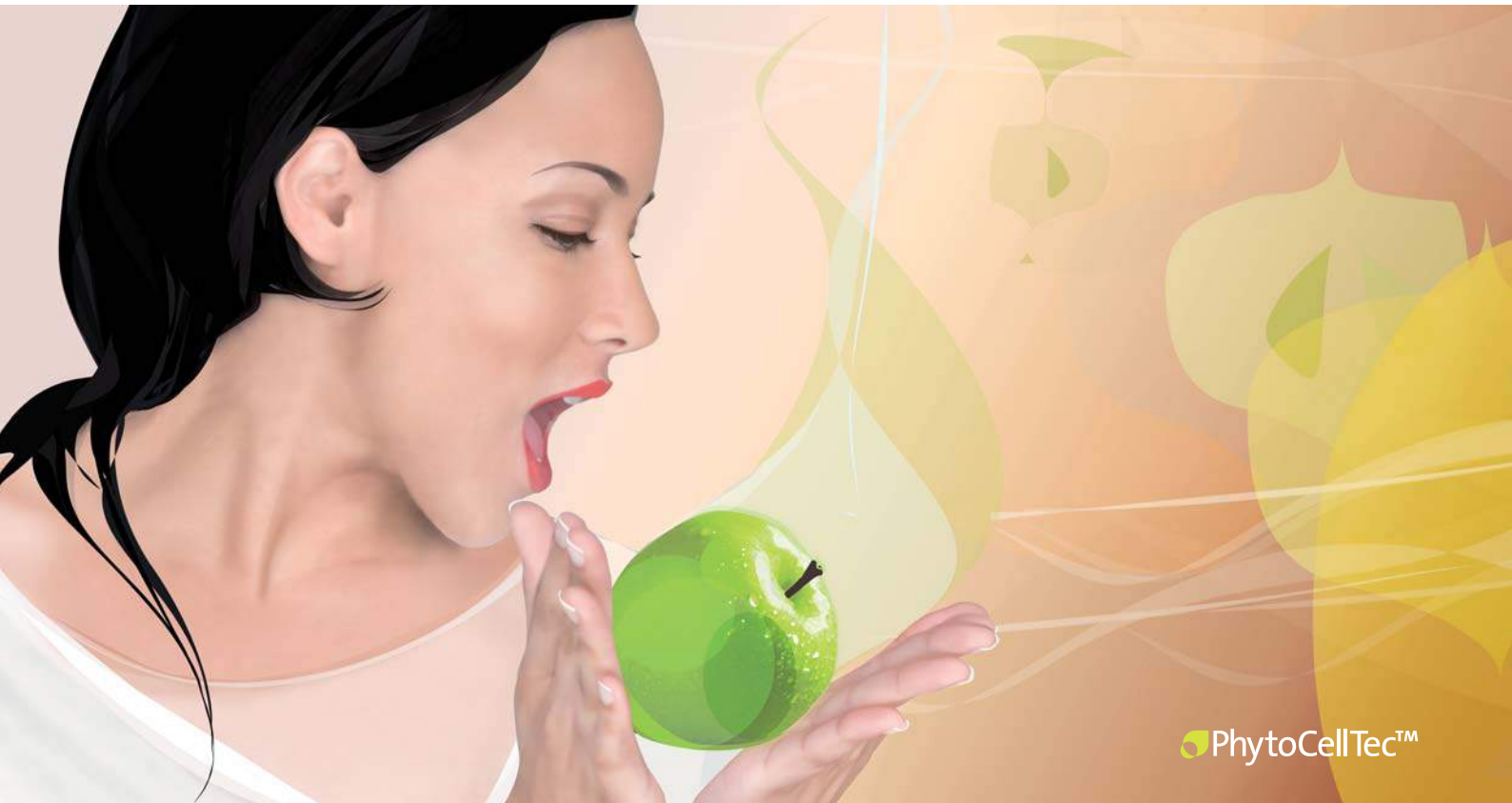
# Clinical Studies

PhytoCell

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mibelle**biochemistry**



PhytoCellTec™



# PhytoCellTec™ Malus Domestica Plant stem cells to protect skin stem cells





# PhytoCellTec™ Malus Domestica

## Plant stem cells to protect skin stem cells

### A Revolutionary Technology to Protect Skin Stem Cells

PhytoCellTec™ Malus Domestica is a liposomal preparation based on the stem cells of a rare Swiss apple.

Uttwiler Spätlauber is an endangered apple variety that was well-known for its excellent storability and thus its longevity potential.

Mibelle Biochemistry has developed a novel technology enabling the cultivation of rare and endangered species like Uttwiler Spätlauber. Thanks to this technology called PhytoCellTec™, plant stem cells can be obtained and incorporated into cosmetic products to ensure the longevity of skin cells.

The protection of human stem cells by PhytoCellTec™ Malus Domestica has been shown by various in-vitro experiments. Other studies demonstrated its age-delaying and anti-wrinkle effects. Thus PhytoCellTec™ Malus Domestica is a revolutionary anti-aging active ingredient based on a high-tech plant cell culture technology.

### Claims with PhytoCellTec™ Malus Domestica

- Protects longevity of skin stem cells
- Delays senescence of essential cells
- Combats chronological aging
- Preserves the youthful look and the vitality of your skin

### Applications

- Skin care products to protect skin stem cells
- Real rejuvenation for face and body care
- Innovative skin care formulations

### Formulating with PhytoCellTec™ Malus Domestica

- Dermatological tolerance: the dermatological tolerance of PhytoCellTec™ Malus Domestica has been carefully proven in healthy volunteers with an occlusive photo-patch test.
- Recommended concentrations: 2–5 %
- Manufacturing of products: PhytoCellTec™ Malus Domestica can be formulated in emulsions (O/W, W/O) and gels. For cold processes, mix PhytoCellTec™ Malus Domestica with the aqueous phase. In cold/hot processes, add during the cooling phase. Homogenization and temperatures of up to 60°C over a short time do not affect the stability of PhytoCellTec™ Malus Domestica.

### INCI/CTFA-Declaration

Malus Domestica Fruit Cell Culture (and) Xanthan Gum (and) Glycerin (and) Lecithin (and) Phenoxyethanol (and) Aqua / Water



# PhytoCellTec™ Malus Domestica

## Swiss apple stem cells to protect skin stem cells

### **A Swiss Apple Variety with Incredible Properties**

Uttwiler Spätlauber is a variety of a Swiss apple that derives from a seedling planted in the middle of the 18th century. It was very famous for its excellent storability without shriveling. Today apple cultivars are selected to maximize crop yield and sweet flavor. Thus Uttwiler Spätlauber with its acid taste is now disappearing.

Uttwiler Spätlauber apples are rich in phytonutrients, proteins and long-living cells. This particular composition leads to incredible storability and longevity properties.

### **Stem Cells and Longevity**

Longevity is related to specific cells called stem cells which have a unique growth characteristic. These unspecialized (undifferentiated) cells can make identical copies of themselves as well as differentiate to become specialized cells. Two basic types of stem cells are present in the human body:

- Embryonic stem cells found in blastocysts can grow and differentiate into one of the more than 220 different cell types which make up the human body.
- Adult stem cells located in some adult tissues can only differentiate into their own or related cell types. These cells act as a repair system for the body but also maintain the normal turnover of regenerative organs such as blood, skin or intestinal tissues.

### **Research on Stem Cells and Applications**

Currently in medicine, adult stem cells are already used particularly in transplant medicine to treat leukemia and severe burns.

In the cosmetic field, scientists are focusing their research on adult stem cells located in the skin. They are studying the potential of this type of cells, their functioning and aging. These researches will help to understand how to protect skin stem cells.

### Stem Cells in the Human Skin

In the human skin, two types of adult stem cells have been identified:

- Epithelial skin stem cells which are located in the basal layer of the epidermis.
- Hair bulge stem cells located in the hair follicle.

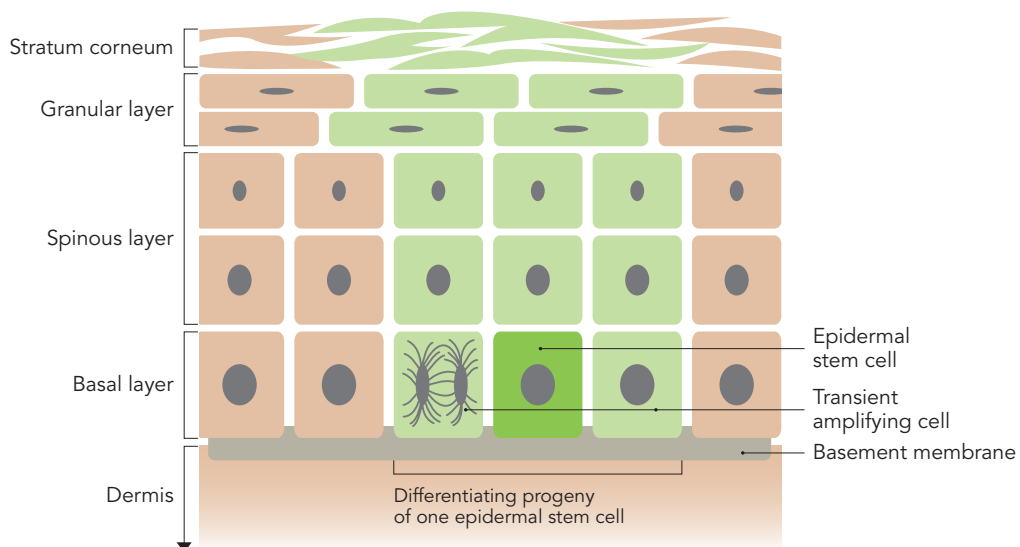
Epidermal stem cells replenish and maintain the balance of cells within the skin tissue and regenerate tissue damages during injury. But with age, the number of skin stem cells decreases and their ability to repair the skin becomes less efficient.

### Plant Stem Cells to Protect Skin Stem Cells

In contrast to human, plant cells are totipotent, meaning that every cell has the ability to regenerate new organs (leave, flower, seed...) or even the whole plant. Besides, all plant cells can dedifferentiate and become a stem cell.

All stem cells, independently of their origin (plant, animal or human) contain specific epigenetic factors whose function is to maintain the self-renewal capacity of stem cells.

## Epidermal Stem Cells in the Human Skin



# PhytoCellTec™

## A high-tech biotechnology to cultivate cells from rare plants

### PhytoCellTec™ by Mibelle Biochemistry

Mibelle Biochemistry developed a novel technology (PCT) enabling the cultivation of cells from rare and endangered plant species. This PCT technology, based on the unique totipotency of plant cells uses the wound healing mechanism of plants. A part of a plant is wounded to induce the formation of callus cells. This wound healing tissue consists of dedifferentiated cells which are stem cells. Callus cells are harvested and cultivated in a suspension and a novel bioreactor system enables a large scale culture. To obtain the PhytoCellTec™ Malus Domestica cosmetic ingredient, these stem cells are harvested and homogenized at 1200 bar together with liposomes to encapsulate and stabilize oil- and water soluble components.

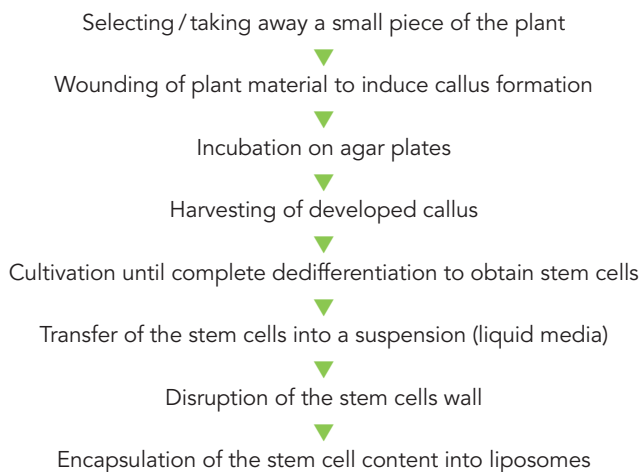
PhytoCellTec™ Malus Domestica is thus rich in epigenetic factors and metabolites which assure the longevity of cells and protect stem cells.

### Advantages of PhytoCellTec™ Technology

This innovative technology developed by Mibelle Biochemistry offers the following advantages:

- Possibility to cultivate cells of rare and endangered plants while respecting the environment
- Availability of plant material independent of the season and market's demand
- Plant material completely free of environmental pollutants and pesticides
- Constant concentrations of metabolites in the stem cells

### PhytoCellTec™ Process



# PhytoCellTec™ Malus Domestica

## Study results

### Maintenance of Stem Cell Growth

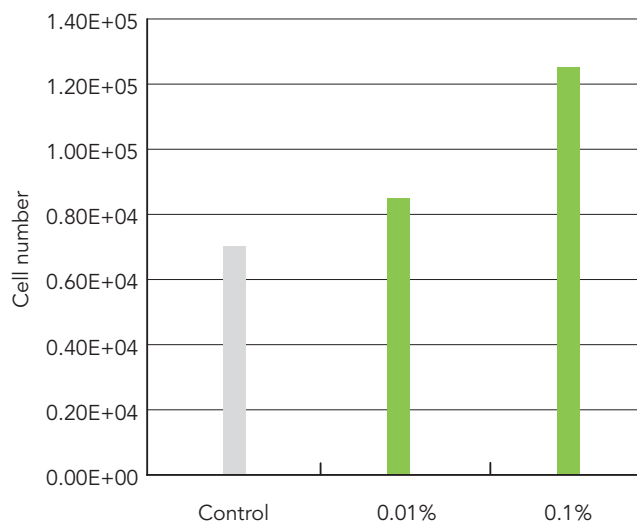
An in-vitro test was conducted on umbilical cord blood stem cells with Malus Domestica stem cell extract which is the active component of PhytoCellTec™ Malus Domestica. Umbilical cord blood stem cells (UCBSC) are the “youngest” safely available stem cells for research.

The influence of Malus Domestica stem cell extract on UCBSC artificial growth was evaluated by counting the cell number after incubation.

Results showed that Malus Domestica stem cell extract has a positive effect on UCBSC's artificial growth thus maintaining the growth and the proliferative activity of UCBSC.

### Maintenance of Stem Cell Growth

■ Malus Domestica stem cell extract



# PhytoCellTec™ Malus Domestica

## Study results

### Protection against UV Radiation

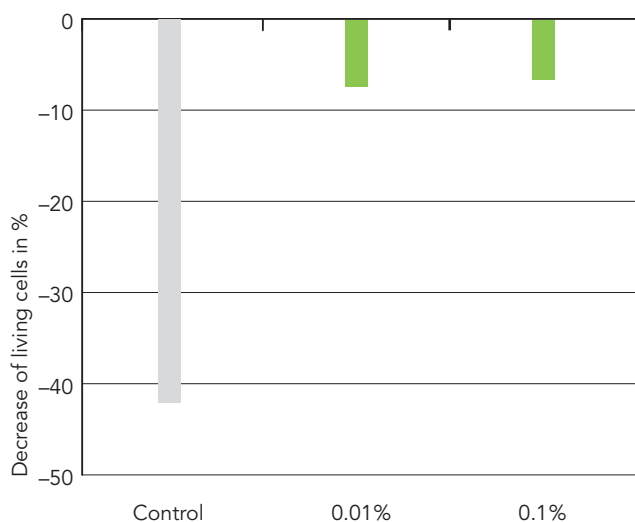
A second in-vitro test was conducted on umbilical cord blood stem cells with Malus Domestica stem cell extract which is the active component of PhytoCellTec™ Malus Domestica.

Results showed the capacity of Malus Domestica stem cell extract to protect UCBSC from UV damage even at low concentrations.

The protective effect against UV damage of Malus Domestica stem cell extract on UCBSC was evaluated by an MTS assay. UCBSC were incubated with different concentrations of Malus Domestica stem cell extract for 24h and were then exposed to UV radiation. The MTS assay, which measures the number of living cells and therefore the damage from UV, was performed 48h after UV radiation.

### Protection of Stem Cells against UV Damage

■ Malus Domestica stem cell extract



**Effect on Gene Expression  
in Senescent Dermal Fibroblasts**

Recently a cellular model for premature senescence was established based on normal human dermal fibroblasts. After a two hours treatment with H<sub>2</sub>O<sub>2</sub> the cells showed the typical signs of senescence. This model was used to prove the anti-senescence effect of the Malus Domestica stem cell extract. After the H<sub>2</sub>O<sub>2</sub> treatment, the fibroblast cells were incubated with a 2% extract for 144 hours. Then gene expression was analyzed with a cDNA array system comprising 150 probes.

Results showed that Malus Domestica stem cell extract can up-regulate specific genes involved in:

- Delay of senescence
- Protection against oxidative stress
- Repair of DNA

**Up-Regulation of Specific Genes involved in the Delay of Senescence**

↓ Gene, that is down regulated by senescence induction (Control)

↑ Gene, that is up regulated or normalized in senescent cells by PhytoCellTec™ Malus Domestica

Genes	after H <sub>2</sub> O <sub>2</sub> Control	after H <sub>2</sub> O <sub>2</sub> + 2 % Malus Domestica stem cell extract
cyclin B1: induces proliferation	73 ↓	130 ↑
cyclin E1: cell cycle regulator	78 ↓	135 ↑
p53: tumor suppressor gene	63 ↓	137 ↑
insulin-like growth factor II: cell proliferation enhancer	71 ↓	117 ↑
heme oxygenase 1: antioxidant enzyme	89 ↓	211 ↑

# PhytoCellTec™ Malus Domestica

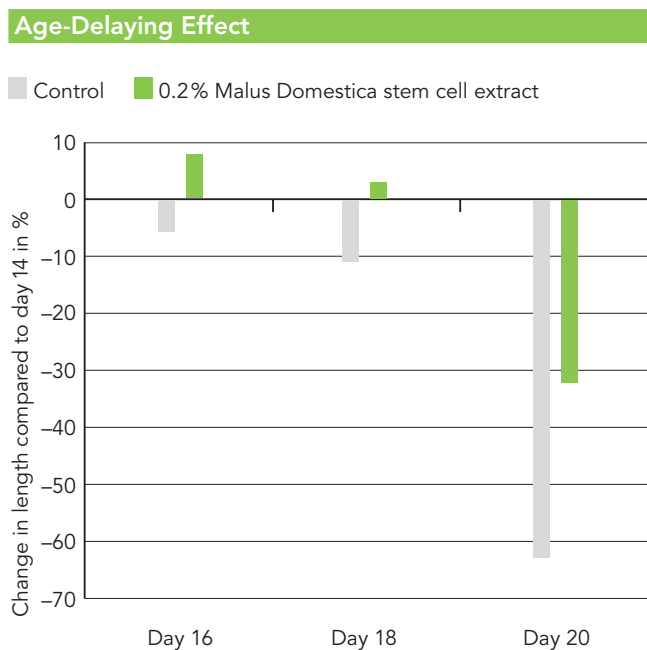
## Study results

### Age-Delaying Effect on Isolated Human Hair Follicles

Human hair follicles can be isolated by microdissection from skin fragments that are left after facelift surgery. Hair follicles are mini organs that represent a natural coculture model of epidermal and melanocyte stem cells and differentiated cells. The follicles can be maintained in a growth medium where they elongate until about day 14. Then the follicle cells gradually become senescent or undergo apoptosis which is a programmed cell death. This necrosis process is caused by the lack of blood circulation. Isolated hair follicles represent a test model to screen for actives that can delay the necrosis process.

Isolated human hair follicles were incubated with Malus Domestica stem cell extract.

Addition of 0.2 % of this extract was found to slightly but clearly postpone senescence- and apoptosis-induced necrosis: follicles kept in presence of the Malus Domestica stem cell extract continued to elongate until day 18, whereas the control follicles started to shrink after day 14.



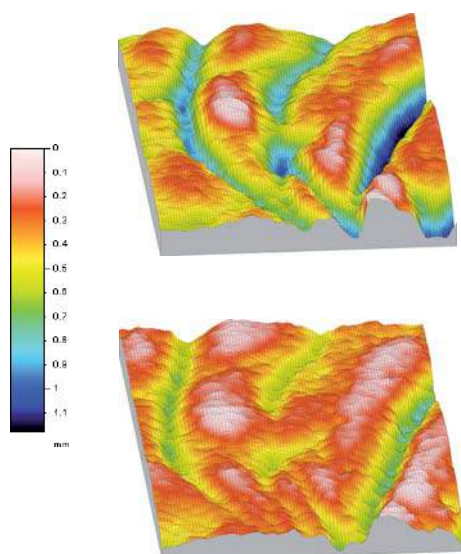
### Anti-Wrinkle Effect on "Crow's Feet"

The anti-wrinkle effect of PhytoCellTec™ Malus Domestica was evaluated in a study with 20 volunteers aged from 37 to 64.

An emulsion containing 2 % of PhytoCellTec™ Malus Domestica was applied twice daily for 28 days to the crow's feet. Wrinkle depth was determined by means of PRIMOS (phase-shifting rapid in vivo measurement of skin).

Results showed a significant and visible decrease in wrinkle depth for 100 % of the subjects.

### Anti-Wrinkle Effect on Crow's Feet



Before  
(day 0)



After  
(day 28)  
2% PhytoCellTec™  
Malus Domestica





# PhytoCellTec™ Malus Domestica

## Plant stem cells for skin stem cell protection

### Claims with PhytoCellTec™ Malus Domestica

- Protects longevity of skin stem cells
- Delays senescence of essential cells
- Combats chronological aging
- Preserves the youthful look and the vitality of your skin

### Applications

- Skin care products to protect skin stem cells
- Real rejuvenation products for face and body care
- Innovative skin care formulations

### Marketing Benefits

- First plant stem cell active ingredient on the market (patent pending)
- Innovation in “stem cells” cosmetics
- Breakthrough in anti-aging

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# Clinical Studies

SYN-EYE



# SYN<sup>®</sup>-EYE

Lineless looking eyes within days





## The windows to the world

It's been said the eye is the window to the outside world. This is why it attracts a lot of attention and it requires a lot of care. With long standing experience in skin care, DSM has created a multifunctional, patented ingredient complex that fulfill consumers' expectation for high- and fast-performing eye care products.

### Key facts

#### Unique product features

- SYN<sup>®</sup>-EYE combines SYN<sup>®</sup>-Peptide know-how with superior ingredients in a multifunctional eye care formula
- It offers multi-target science based approach to fight against the most common concern in eye care – the appearance of lines & wrinkles and dark circles
- It shows significant effects in only 7 days
- SYN<sup>®</sup>-EYE is a patented complex and fully China compliant

#### Benefits

- Reduces visibly the appearance of lines and wrinkles around the eye within 7 days
- Reduces the appearance of dark circles
- Improves the skin's texture and smooths the delicate skin eye area
- Moisturizes, protects, and energizes the skin around the eyes

#### Cosmetic applications

- Fast-acting and multi-functional eye care formulas
- Anti-aging eye care products to minimize the visual aspect of lines and wrinkles
- Product that focuses on youthful, fresh, and smooth facial skin
- Product that reduces the appearance of dark circles

#### Suggested concentration

1% SYN<sup>®</sup>-EYE

#### INCI name (active)

Palmitoyl Tripeptide-5, Panthenol, Sodium Hyaluronate, Algae (*Dunaliella Salina*) extract



### Need for multifunctional products

The eye area ages faster as it is the thinnest and most fragile area of skin. Over the years the production of collagen slows down and an extensive muscle contraction contributes to the formation of lines and wrinkles.

The delicate area around the eyes needs special care and focus on different parameters, such as collagen reduction, microcirculation and skin thinning, all of which needs to be taken care of.

Most of the products in the market only treat one aspect and disregard others. However, the multifunctionality of SYN<sup>®</sup>-EYE offers more opportunity to maintain this sensitive area in an effective and gentle way. This multifunctionality is highly accredited in consumer feedback.

**48% of global skin care shoppers** found it important or very important to **minimize the number of products** used in their health and beauty regime.\*\*



**71% said multifunctional products are convenient and time saving.\***



**68% said multifunctional products save me money instead of buying multiple products.\***



**66% said multifunctional products allow me to reduce or replace the number of skincare products I use.\***



# SYN<sup>®</sup>-EYE – 4 in 1 blend *in vivo* efficacy

Effect on wrinkles and fine lines



High consumer acceptance



Effect on dark circles



Significant in 7 days



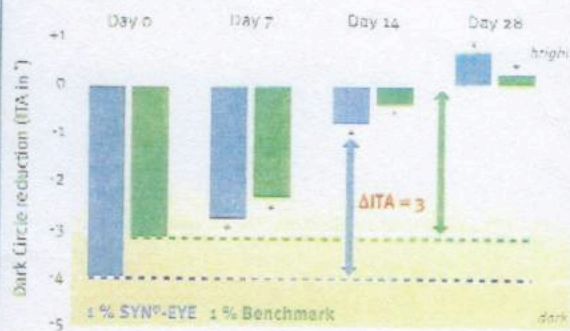
SYN<sup>®</sup>-EYE efficacy was evaluated in a 4 week, split-face study amongst European female volunteers in the age range of 35-55.

It compared 2 samples (SYN<sup>®</sup>-EYE and a competitive benchmark)\*\* against a placebo in an eye care cream.

Measurement of different parameters on wrinkle and dark circles has been conducted by Primos or DermaTop; image analysis has been performed by Newton

Visible difference in skin color in the dark circle area

**Result:** SYN<sup>®</sup>-EYE shows a visibly brighter skin color in dark circle area after only 14 days.

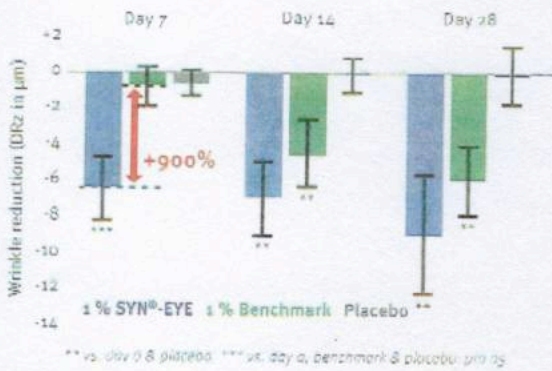




## Continuous visible improvement on fine lines and wrinkles

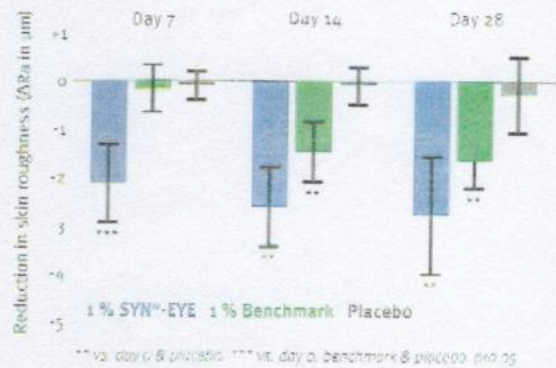


Significant reduction in the appearance of wrinkles compared to benchmark and placebo



**Result:** SYN®-EYE shows a significant anti-wrinkle appearance in 7 days.

Smoothing – noticeable reduction in roughness compared to day 0

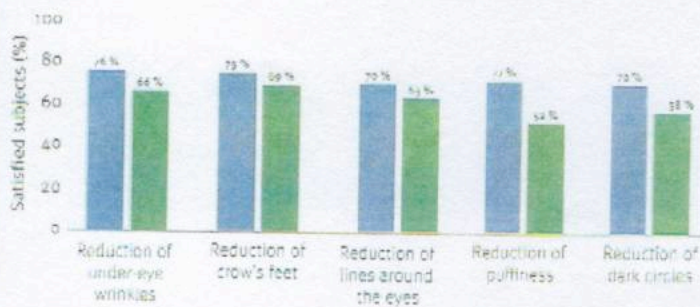


**Result:** SYN®-EYE shows a significant effect on the appearance of smoother skin in only 7 days.

### Let's ask the consumer!

Consumer questionnaire: products efficacy on wrinkles

Consumers confirmed outstanding activity of SYN®-EYE



**Result:** Higher consumer acceptance in all key aspects compared to benchmark.



# SYN<sup>®</sup>-EYE: 4-in-1 blend composition

## Palm-Lys-Val-Lys-OH\*

Palm-Lys-Val-Lys-OH is a small synthetic tripeptide with a unique sequence that imitates the human body's own mechanism to reduce the appearance of fine lines and wrinkles.

### Key benefits:

- Protects from collagen network from the appearance of degradation
- Boosts smoother, firmer skin

## Dunaliella salina extract\*

*Dunaliella salina* is a very small unicellular microalgae, discovered in 1838 by Dunat in the salters of Montpellier. It grows in salt water with up to 30% salinity which is nine times higher than sea water. Living in such harsh conditions, *D. salina* has become an expert of surviving. This feature, based on a powerful cocktail of different metabolites such as amino acids and carbohydrates, qualifies *D. Salina* as a unique ingredient to reload the skin with new energy.

### Key benefits:

- Energizes and protects *in vitro* mitochondria
- Stimulates *in vitro* epidermal renewal

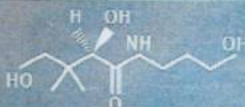


## Panthenol\*

Pro Vitamin B5 or D-Panthenol has been used for years in hair care products. It functions as a Humectant, increasing the water content in hair and improves its elasticity. When applied to the skin D-Panthenol readily converts to pantothenic acid. Pantothenic acid, also known as vitamin B5, is part of the B group vitamins and is classified as a water-soluble vitamin. Panthenol itself can also attract water into the upper layer of the skin and can enhance the regenerative appearance of skin.

### Key benefits:

- Helps to keep the skin moist and supple
- Inhibits the appearance of irritation and redness



## Hyaluronic acid

Hyaluronic acid (HA) is a non-branched, naturally occurring polysaccharide of the human body. It is mainly found in the extracellular matrix. HA today is mainly produced by fermentation, followed by an extended purification. During the process special attention is paid to maintain a particular molecular size range (350 to 550 kD) to ensure the best combination between film forming properties and anti-aging benefits.

### Key benefits:

- Excellent moisturizing benefit
- Anti-wrinkle and firming effect

