mibelle GROUP biochemistry

CPCIA PERSONAL CARE INGREDIENTS
INNOVATION PRIZE 2013
BEST ANTI-AGING INGREDIENT

DermCom

Cell2cell communication for skin matrix repair

SWISS QUALITY PRODUCT

DermCom
Cell2cell communication for skin matrix repair

A Flower Bulb Extract to Improve Cell-Cell Communication
Based on a Crocus chrysanthus bulb extract, DermCom can reverse the aging process by stimulating the communication between skin cells.

The crocus is a universal symbol of rejuvenation and youthfulness. Crocus chrysanthus "Cream Beauty" is a beautiful variety with creamy-colored petals. Bulbs are plant parts specializing in the storage of nutrients and so are an interesting source of active ingredients for cosmetics.

With age, the communication process between skin cells, which is mediated by growth factors, is reduced. This strongly affects the extracellular matrix (ECM), the structural network of the skin and leads to a reduction of its firmness, elasticity and density.

DermCom was shown, in a series of tests, to stimulate keratinocytes to secrete growth factors that could enhance the synthesis of collagen and elastin in the dermis. This effect on fibroblasts was comparable to the one of the transforming growth factor (TGF-β), a natural growth factor involved in ECM synthesis.

Clinical studies confirmed this result after only 2 weeks' treatment:
- skin firmness was greatly improved
- the collagen and elastin contents in the skin were both increased.

DermCom can thus rejuvenate the skin matrix thanks to its growth factor-like activity and so preserve and improve the biomechanical properties of the skin as well as its quality.

Claim Ideas for DermCom
- Boosts collagen and elastin production
- Stimulates natural growth factors of the skin
- Renews the skin's resilience and firmness
- Reverses aging processes
- Rejuvenates skin texture

Applications
- Collagen and elastin boosters
- Firming and lifting products
- Repair formulas
- Intense anti-aging treatments

Formulating with DermCom
- Recommended use level: 0.4–2%
- Incorporation: Dissolve DermCom into the aqueous phase or add pre-solved (DermCom is easily soluble in water at room temperature) during the cooling phase (< 60 °C).
- Thermostability: Temperatures of up to 60 °C for a short time do not affect the stability of DermCom.

INCI / CTFA-Declaration
Crocus Chrysanthus Bulb Extract (and) Acacia Senegal Gum (and) Aqua / Water

Skin Aging
Growth factors synthesis is reduced with age

Age Depletes the Communication Process between Cells
Fibroblasts, the major cells of the dermis are capable of sending and receiving messages from other skin cells using growth factors and cytokines as messengers. This dialogue is essential for skin regeneration, repair and for growth of the tissues. Released by the cells, these messengers reach their target cells by diffusion and bind them thanks to specific surface receptors.

With age, this communication process is reduced. This strongly affects the extracellular matrix (ECM), the structural network which supports the skin and provides it with its biomechanical properties (firmness, elasticity) as well as its thickness and density.

The Reduced Synthesis of Natural Growth Factors Affects the Skin's Structural Network
Due to the reduced release of growth factors, the activity of fibroblasts decreases; they synthesize less collagen and elastin, the two major proteins which form the ECM, but generate more matrix metalloproteinases (MMP) which degrade the existing matrix. This leads to an imbalance in the renewal of ECM since its degradation surpasses its neosynthesis. This causes important alterations in the skin (loss in firmness, elasticity and density resulting in skin sagging and thinning).

Reaching Fibroblasts via Intercellular Communication
Dermal fibroblasts cannot be reached easily by topically applied cosmetics. However, as these cells communicate with the keratinocytes which are in the outer skin layers, they could be reached using this communication process – a new strategy for cosmetics.

DermCom

A flower bulb extract with a growth factor-like activity to repair the skin matrix

"Cream Beauty" Crocus Bulb, a New Source for Cosmetics

Bulbs are plant parts specializing in the storage of nutrients used to generate a new plant after a low-temperature-induced dormancy period.

Crocus chrysanthus bulbs were selected from several bulb plants for their safety, availability and activity on the skin.

Crocus is actually a bulb-like plant; contrary to real bulbs (e.g. tulips) that store nutrients in modified leaves, crocus is a corm meaning that it stores nutrients in the modified stem.

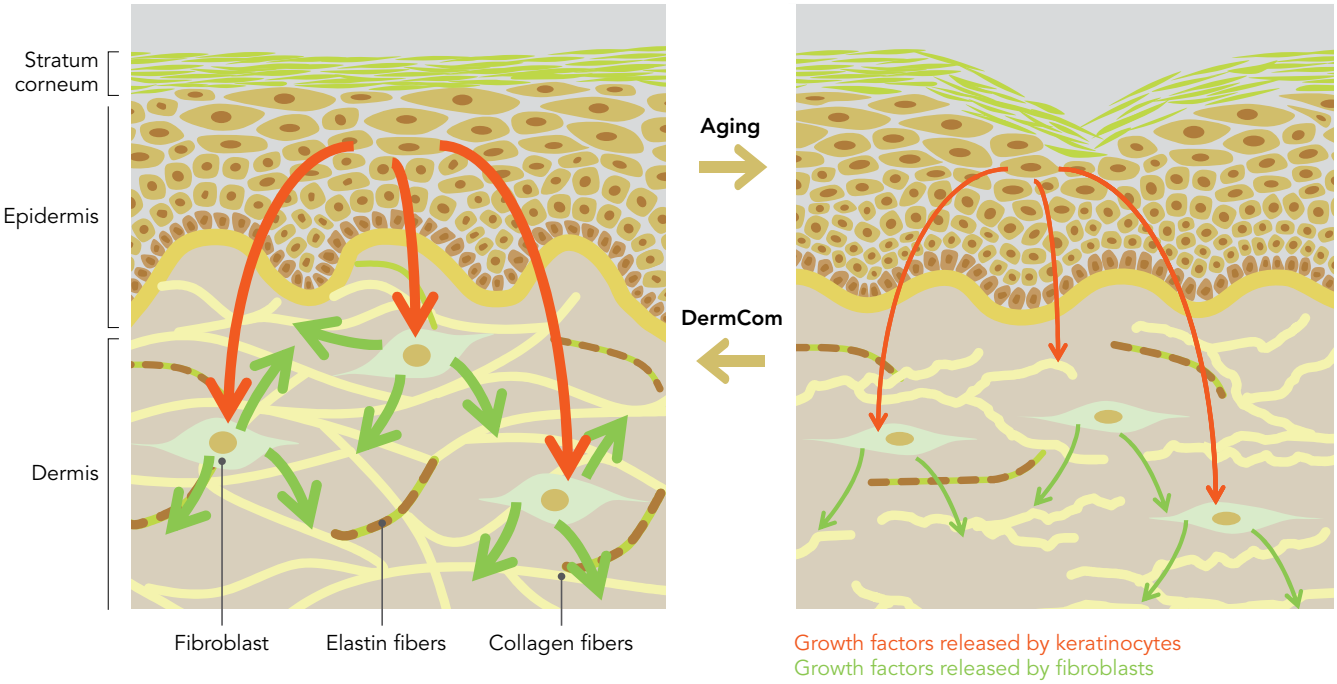
As an early spring-flowering plant, Crocus chrysanthus is a universal symbol of rejuvenation and youthfulness. This species grows in the mountains of southern Europe. Its attractive cultivar "Cream Beauty" owes its name to its creamy yellow petals contrasting with its bright orange center.

DermCom Mimics the Activity of Natural Growth Factors in the Dermis

An active ingredient was developed from a Crocus chrysanthus bulb extract. DermCom, the resulting product, was shown in a series of tests to stimulate keratinocytes to secrete growth factors that could enhance the synthesis of matrix proteins in the dermis.

Its activity on fibroblasts was comparable to the one of the transforming growth factor (TGF-β) which activates the synthesis of ECM proteins (collagen and elastin). DermCom has thus a growth factor-like activity in the dermis.

Mechanism of DermCom



DermCom
Study results

Effect on Epidermal – Dermal Cell-Cell Communication

The effect of DermCom on keratinocyte-fibroblast communication was evaluated using DNA microarray technology and was compared to the TGF-β growth factor one.

For this, gene array analysis was conducted on:

- keratinocytes and fibroblasts "directly" treated with DermCom
- fibroblasts "indirectly" treated with DermCom in order to mimic the reality. For this, fibroblasts were incubated with the secretions of keratinocytes treated first with DermCom.

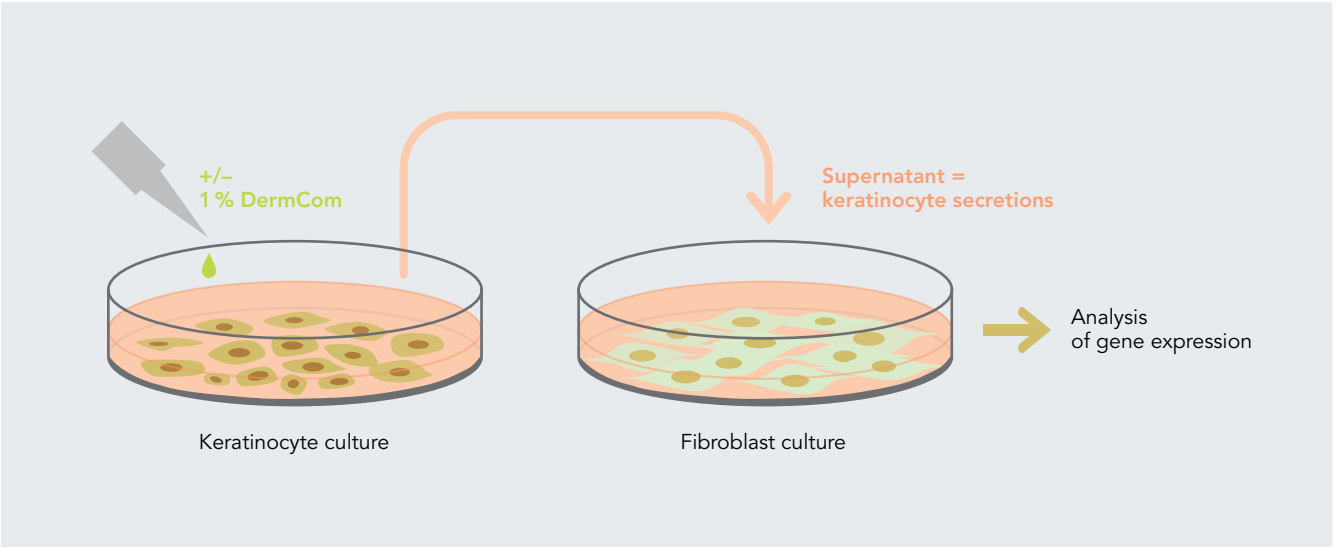
Keratinocytes from a 50 year old donor were treated or not with DermCom. The cell cultures were then centrifuged to separate the cell pellets from the supernatant (keratinocyte secretions). Then, the keratinocyte cells were washed and the expression of growth factors typically expressed in these cells was analyzed by quantitative PCR.

Fibroblasts of a pool of donors over 50 years old were treated or not with:

- the previously obtained secretions of the untreated keratinocytes (control)
- the previously obtained secretions of the DermCom-treated keratinocytes
- TGF-β (external positive control)
- DermCom (direct control).

At the end of the incubation, fibroblast cells were washed. The expression of matrix proteins in these cells was analyzed by quantitative PCR.

Study Design

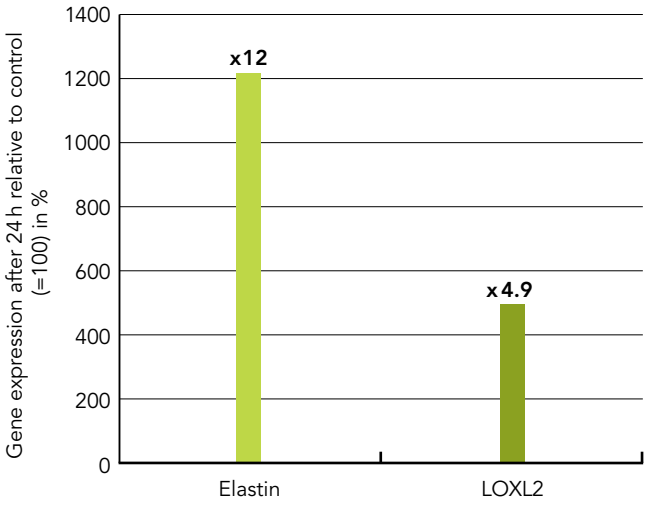


Growth Factor-Like Activity

Gene expression analysis conducted on fibroblasts incubated with the test products for 24 h showed that:

- secretions of untreated keratinocytes (coming from a 50 year old donor) had a pro-aging effect on fibroblasts (control). This resulted in a reduced expression of elastin and lysyl oxidase-like 2 (LOXL-2), an enzyme required for elastic fiber formation.
- DermCom, when applied directly to the fibroblasts, had no effect or a slight pro-aging effect on these cells.
- as expected, TGF-β had an anti-aging effect on fibroblasts as it led to a strongly increased expression of elastin and LOXL-2.
- secretions of keratinocytes treated with DermCom had a strong anti-aging effect comparable to the TGF-β's one.

Stimulation of Elastin Fiber Formation in Fibroblasts



DermCom
Study results

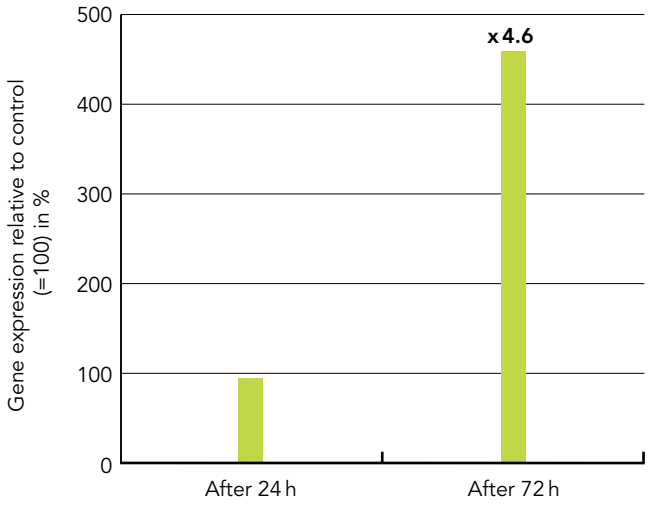
During the previously described study, the gene expression coding for the connective tissue growth factor (CTGF) was also analyzed in fibroblasts after 24 h and 72 h of incubation with the different test products. CTGF stimulates the production of collagen by fibroblasts and is significantly reduced in aged skin.

Secretions of untreated keratinocytes showed an aging effect by significantly reducing CTGF expression. However, here also, secretions of keratinocytes treated with DermCom had a similar effect to TGF-β and led to an increased expression of CTGF.

This indicates that the stimulatory effect of DermCom on the synthesis of matrix proteins is due to the compounds secreted by the keratinocytes when they are first treated with DermCom.

DermCom can thus reverse the aging process by stimulating the communication between keratinocytes and fibroblasts in aged skin.

Stimulation of CTGF in Fibroblasts



Gene array analysis conducted on keratinocytes showed that DermCom increased the expression of growth factors playing an important role in keratinocyte growth, tissue repair and communication between the epidermis and the dermis:

- fibroblast growth factor 5 (FGF-5)
- fibroblast growth factor 7 (FGF-7)
- connective tissue growth factor (CTGF)
- insulin-like growth factor binding protein 6 (ILGFBP6).

Thus, the anti-aging effect of DermCom relies on the stimulation of the keratinocytes to release growth factors. And these growth factors are able to enhance the synthesis of matrix proteins in the dermis as shown in the previous steps of the study.

Stimulation of Growth Factors in Keratinocytes

DermCom
Study results

Matrix' Rejuvenation after 2 Weeks of Treatment

A cream containing 0.4 % DermCom was applied twice daily to the inner side of the forearm of a 53 year old woman whilst her other forearm was treated with the corresponding placebo.

Analysis of skin matrix was performed using a two-photon microscopy. This innovative non-invasive 3D technique visualizes deeper skin structures. It is based on the principle that infrared laser irradiation can cause autofluorescence of some molecules (e.g. elastin) or second harmonic generation (e.g. collagen).

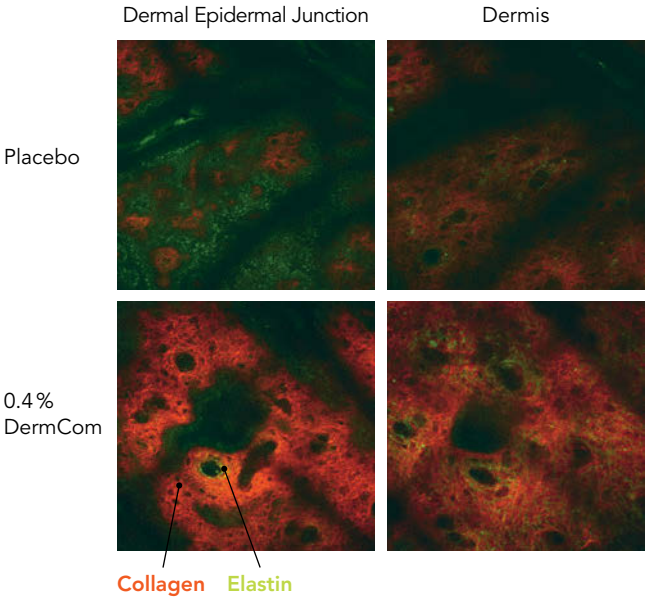
Collagen and elastin were visualized before and after 2 weeks of treatment and their content was measured in the papillary dermis and in the upper part of the reticular dermis.

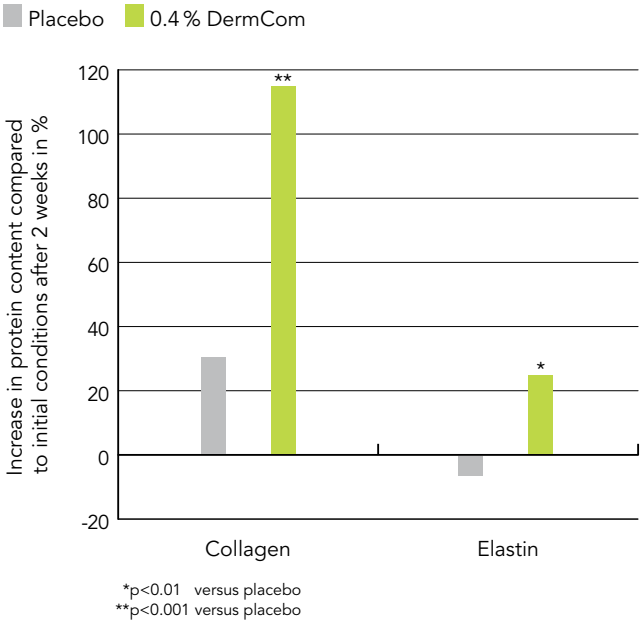
Results showed, already after two weeks' treatment, that DermCom increased the content of the two main skin structure components compared to the placebo:

- by more than 115 %** for collagen
- by more than 25 %*** for elastin.

**p<0.001, ***p<0.01

Increase in Collagen and Elastin Contents





*p<0.01 versus placebo
**p<0.001 versus placebo

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Firming Effect after 2 Weeks of Treatment

20 women aged from 36 to 65 (average: 47.1) applied a cream containing or not 2 % DermCom twice daily for 28 days to the inner side of their forearms. The firmness of their skin was determined using a cutometer.

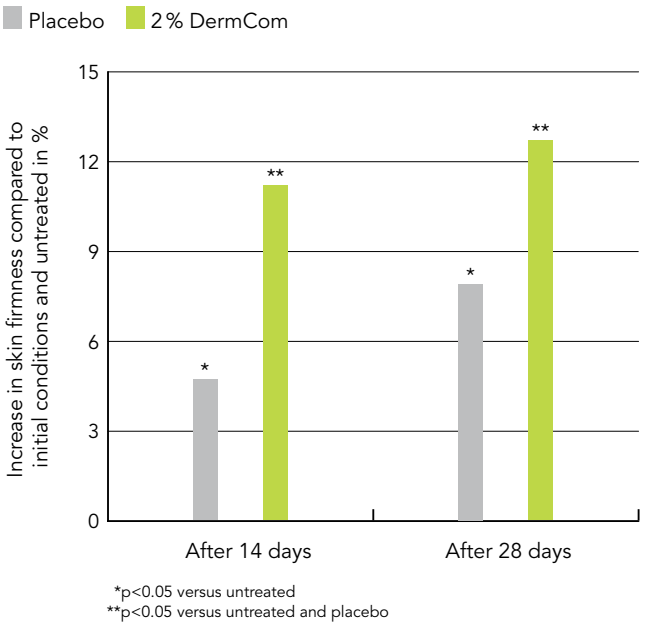
Results showed that DermCom significantly increased skin firmness:

- by more than 11 %** after 14 days
- by almost 13 %** after 28 days.

**p<0.05 versus untreated and placebo

DermCom offers thus a rapid firming effect to the skin.

Increase in Firmness



*p<0.05 versus untreated
**p<0.05 versus untreated and placebo

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Marketing Benefits

- Four time innovation prize winner:
  Innovation Zone Best Ingredient Award in-cosmetics Europe
  Innovation Zone Best Ingredient Award in-cosmetics Asia
  BSB Innovation Prize
  CPCIA Personal Care Ingredients
- Based on a flower bulb, an interesting source for cosmetics
- An advanced strategy to successfully rejuvenate the skin matrix deep in the dermis
- 100% natural origin

Innovating for your success

Mibelle Biochemistry designs and develops innovative, high-quality actives based on naturally derived compounds and profound scientific know-how. Inspired by nature – Realized by science.

Mibelle AG Biochemistry, 5033 Buchs/Switzerland, Phone +41 (0)62 836 17 31, info@mibellebiochemistry.com, www.mibellebiochemistry.com