



biochemistry

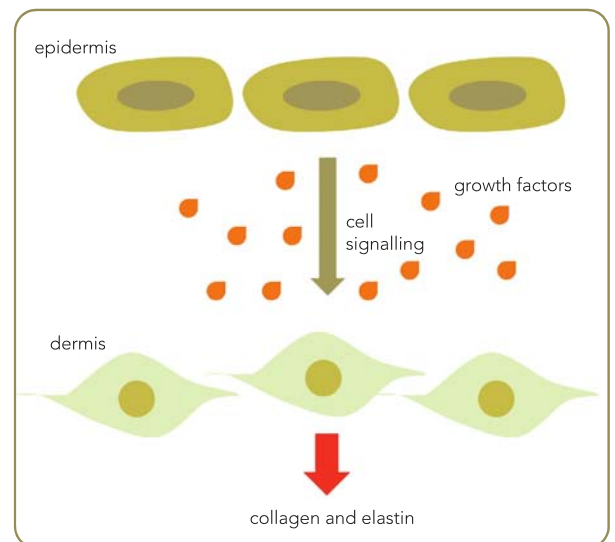
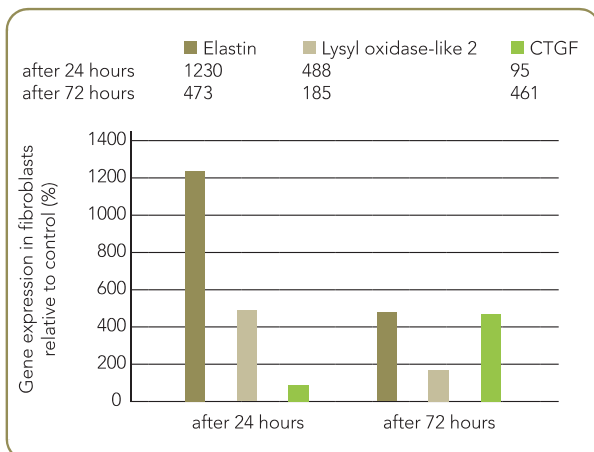
DermCom - to deliver the message for repair deep in the skin

Use of the skin's own communication mechanism between epidermis and dermis for rejuvenation

Cosmetic products work at the skin's surface. There, keratinocyte cells form the epidermis, the skin layer responsible for the barrier function. Another type of cells, called fibroblast, build the underlying skin layer, called the dermis. Fibroblast cells produce the collagen and elastin fibres. The dermis is important for skin firmness and elasticity. Typical signs of skin ageing, like sagging and wrinkles, develop in the dermis. Fibroblasts of old skin can only synthesise collagen and elastin on a very reduced scale. Cosmetic ingredients can easily penetrate into the outer part of the epidermis but their access to the dermis is extremely limited. A strategy for the medication of the ageing dermis by cosmetic treatments could be to utilise the communication processes between the cells of the outer epidermis and the cells of the subjacent dermis. In this way, one could instruct fibroblast cells to activate the synthesis of collagen and elastin fibres.

Epidermis – dermis communication is mediated by growth factors

Communication between epidermis and dermis is mediated by messenger compounds. The messengers are proteins, known as growth factors. They are released by keratinocytes and migrate by diffusion to fibroblasts where they bind to their receptors on the cell surface. The process is known as cell signalling. Depending on the nature of the messenger compound, they can induce specific reactions of the target cell. Cell signalling is a general process used by tissues to adapt to changes in the surroundings. The right active to correct the diminished formation of fibres in the dermis should trigger keratinocytes to release growth factors that communicate to fibroblasts to





enhance the formation of collagen and elastin. Finally, the skin will be repaired and regenerated from inside.

Bulbs of crocus chrysanthus trigger the right communication

Cell culture assays with keratinocytes and fibroblasts were used to screen plant extracts for the right communication triggers. Keratinocyte cultures were incubated with the plant extracts. After separation of the cells, the medium supernatant containing the released messenger compounds, was used to incubate fibroblast cells in it. After incubation, the activity of selected fibroblast genes was analysed. The medium supernatant of keratinocytes incubated in an extract of crocus chrysanthus bulbs was found to strongly activate the formation of elastin, of the elastin fibre-synthesising enzyme and of the connective tissue growth factor (CTGF). Analysis of the keratinocyte medium supernatant confirmed that the extract induced the release of messenger compounds such as fibroblast growth factors and also CTGF. The newest literature shows that CTGF becomes a limiting factor in ageing skin and that a boost in CTGF might increase collagen content. These results demonstrate that in fact an extract of crocus bulbs could trigger the right communication to correct age-related loss of fibre production in the dermis.

Increase of collagen amount by 115% after two weeks' application

Two clinical studies showed that the concept demonstrated in cell culture assays works in real skin. In a first clinical pilot trial, two-photon microscopy, a non-invasive analytical tool, was used to measure collagen and elastin in the dermis. The amount of both fibres was clearly increased compared to the placebo already after two weeks' application of a cream with 0.4% of the crocus bulb extract. The two-photon microscopy pictures

showed also qualitative differences between verum and placebo treated skin. The verum was found to clearly reduce the size of wrinkles. The wrinkles in the placebo treated skin zone are visible as dark, crack-like openings that are wide at a depth of 12 microns and become narrower at 24 and 48 micron depths. By contrast, there was a complete absence of such dark openings, even in the superficial layers, in the verum treated skin. In another clinical study with 20 women over 4 weeks, a cream with 2% of the crocus bulb extract clearly improved skin firmness and elasticity and reduced wrinkles in the crow's feet area.

