



DOES IT REALLY WORK?

CBD | During the last years, cannabidiol has gained increasing interest in the world of cosmetics. Not all skin benefit claims, however, are based on efficacy studies and consumers wonder whether it really has a positive influence on the skin. Dr Katharina Kappler reports on the latest results on the effects of CBD in cosmetics.



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As a trend ingredient in many skin care products worldwide, CBD promises skin soothing and relaxation, as well as a reduction of skin redness and inflammation. Not all skin benefit claims, however, are based on efficacy studies and consumers wonder whether it really has a positive influence on the skin. Indeed, CBD provides numerous health benefits. In 2018, the

FDA approved the first prescription drug based on CBD for the treatment of epileptic seizures¹. Moreover, ingestion or inhalation is used to treat anxiety, depression, chronic pain, and insomnia². The biochemical function is well understood for these systemic applications, but the effects for topical CBD applications are still less clear.

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Proven effects on the skin

Several studies have proven the successful absorption of topically applied CBD into the skin³. Due to the hydrophobic nature, appropriate carrier systems, however, are necessary to allow efficient uptake into the skin. Within the skin, the existence of the endocannabinoid system provides a plausible explanation of how CBD could lead to the claimed effects.

The **endocannabinoid system** is a signalling network that has been mainly described to modulate the central nervous system and immune functions, but it also exists in the skin, where nine endocannabinoids are present⁴. The main targets for cannabinoids in the nervous system – cannabinoid receptor 1 and 2 – as well as additional targets for cannabinoids, such as transient receptor potential (TRP) and peroxisome

proliferator activated (PPA) receptors, are expressed in different skin cells, including fibroblasts and keratinocytes³. Even though the signalling pathways of the endocannabinoid system could explain some of the CBD effects in the skin, there are only a few publications, which prove these functions. Based on literature research, we have identified four major effects of CBD in the skin:

- **Antioxidant function:** CBD increases the expression of antioxidant genes, such as HMOX1, by stimulating the transcription factor NRF2 in human keratinocytes^{5,6}. Furthermore, it prevents lipid peroxidation and protects from hydrogen peroxide-induced oxidative stress and cell death^{6,7}.
- **Anti-inflammatory properties:** CBD can inhibit the pro-inflammatory transcription factor NF-κB and thereby modulate inflammation in UVA-irradiated keratinocytes⁶. It has been suggested that CBD inhibits NF-κB mainly via the activation of receptor PPARγ⁸.
- **Soothing effect:** CBD can desensitise TRPV1 (TRP Vanilloid-1), a pain receptor that is expressed in nerve fibres but also in keratinocytes and can thereby potentially lead to pain relief and skin soothing⁹.
- **Wound healing improvement:** Topical application of CBD was shown to increase the expression of cytokeratin genes KRT16 and KRT17, which are associated with

keratinocyte proliferation and wound repair⁵.

Due to these positive effects on the skin and the ability to regulate lipid production^{10,11}, CBD has been discussed for the treatment of acne, seborrhoea, eczema, and atopic dermatitis³, even though additional studies are needed to confirm its efficacy.

Synergistic effects with Swiss stone pine extract

For our own studies, we used purified CBD, which was encapsulated into a nano emulsion using organic hemp seed oil. This step not only improves the water solubility of CBD, but also increases the bioavailability in the skin. The encapsulated CBD was then combined with a Swiss stone pine (*Pinus cembra*) extract for a synergistic effect.

The Swiss stone pine, a tree that grows in high altitudes, is notably rich in the molecule pinosylvin, a stilbenoid like resveratrol, which is known to reduce inflammation and neutralise free radicals. This combination, called CBD + pinosylvin¹² in the following, was tested in several studies to investigate the effect on skin inflammation, wound healing, and facial relaxation.

The **anti-inflammatory activity** of CBD + pinosylvin was measured in human keratinocytes by the release of prostaglandin E2 (PGE2), a potent pro-inflammatory mediator. Cells were treated either with the combination of ingredients before induction of ▶



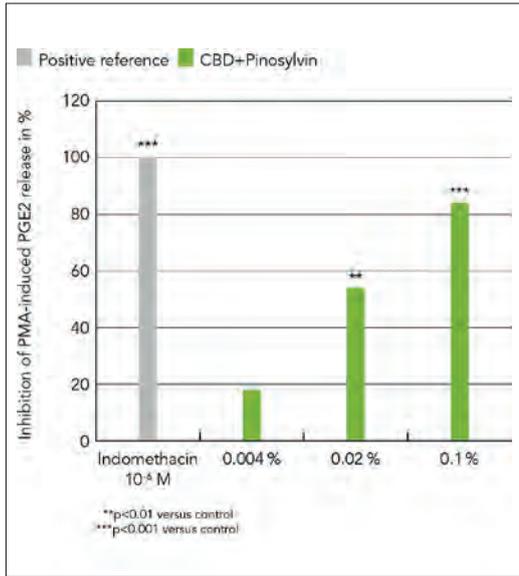


figure 1: Inhibition of inflammation induced PGE2 release by treatment with CBD+pinosylvin.

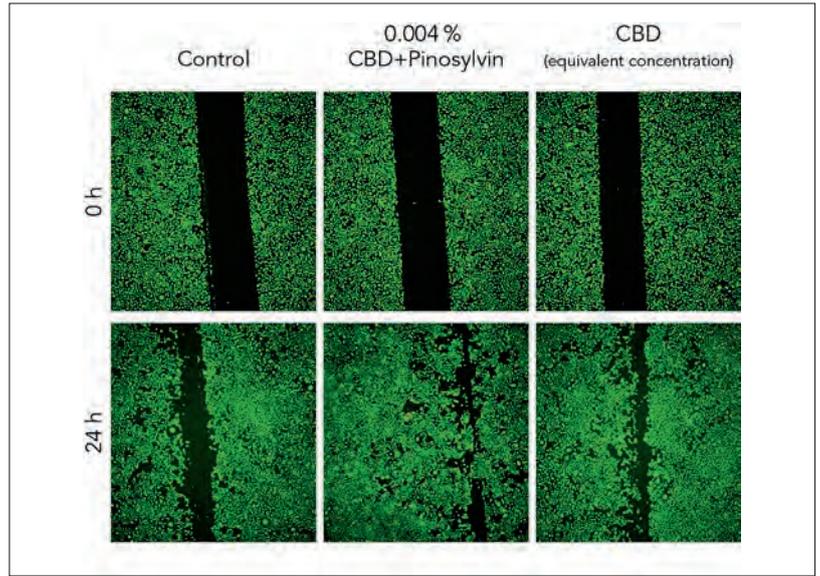


figure 2: Increased speed of tissue regeneration after treatment with CBD or CBD+ pinosylvin.

inflammation by phorbol myristate acetate and measurement of PGE2 in the supernatant of the cells. The treatment with the ingredient's combination inhibited PGE2 release dose-dependently with a maximal inhibition of 84% at the highest concentration of 0.1% (figure 1). This inhibitory effect was comparable to that of indomethacin, an established inhibitor of PGE2 release. Thus, the treatment with CBD + pinosylvin can reduce inflammation in the skin, which could also lead to a reduction in skin redness, as PGE2 release leads to vasodilation.

To test the **wound healing capacity** of CBD + pinosylvin, a scratch assay was performed in human keratinocytes treated with either 0.004% of the combination of the ingredients or an equivalent concentration of CBD in DMSO. While both treatments had a positive effect on cell proliferation, the combination accelerated wound healing more strongly than CBD alone (figure 2). A possible explanation for this observation is the synergistic activity of CBD and the Swiss stone pine extract as well as the increased bioavailability of the encapsulated CBD.

In a placebo-controlled clinical study with 41 volunteers (38-65 years), the skin roughness on the subjects' cheeks and the number of wrinkles

in the crow's feet area were measured to investigate the **effect of smoothing the skin texture due to facial relaxation**. The volunteers were split into two groups and used either a cream with 2% CBD + pinosylvin or a corresponding placebo cream on the face twice daily for 28 days. The treatment with the combination of ingredients led to a significant reduction of the number of wrinkles by 28% and skin roughness by 6.5% (figure 3). In addition, the relaxing effect was analysed using an image-based method, which visualises all changes on the skin surface that occur during the treatment. The most remarkable differences were along the jawline, where an upward movement was observed, and on the cheeks, where the volume of the skin surface was slightly increased.

In the same study, **skin colour** was analysed using a technology that detects **vascular structures and hyper-pigmented spots** and quantifies the red and brown colour intensities. Compared to initial conditions, treatment with 2% CBD + pinosylvin led to a significant reduction of the clusters of melanin and haemoglobin by 13.7% and 17.8% after 28 days, which was also visible in representative images taken of the volunteers (figure 4). As both chromophores, haemoglobin, and melanin, can be

stimulated by oxidative stress and inflammation, the improvement of the skin tone can be attributed to the anti-inflammatory and antioxidant effects of the combination of ingredients.

Conclusion

Using the right formulation, CBD can be delivered into the skin, where a functional endocannabinoid system exists, which provides the molecular basis for its efficacy in the skin. Indeed, several in vitro studies have shown the anti-inflammatory, antioxidant, soothing and wound healing capacity of CBD in different skin models. These effects of CBD can be enhanced by combined synergistic treatments.

Correctly formulated CBD can exert beneficial effects on the skin and is a promising ingredient for cosmetic applications. □

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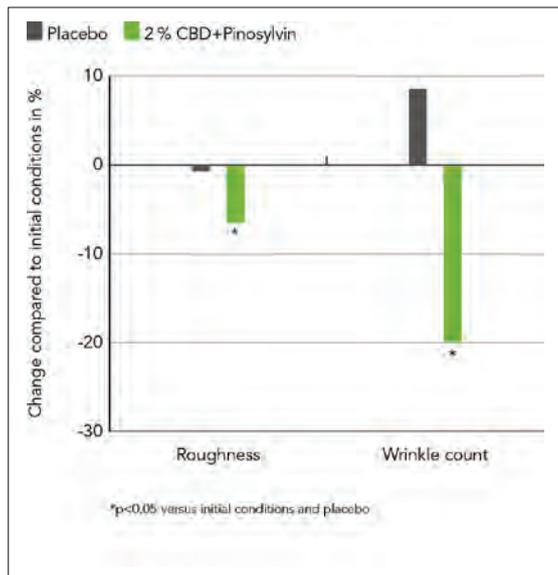


figure 3: Reduction of skin roughness and wrinkles after treatment with CBD+pinosylvin.

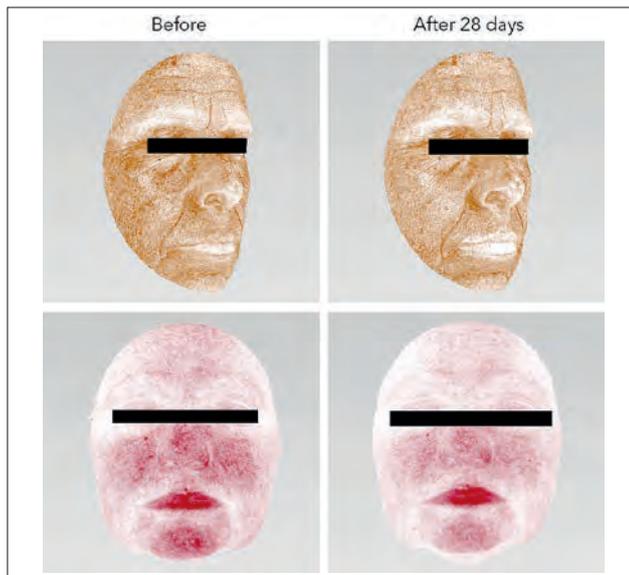


figure 4: Reduction of hyperpigmented spots and skin redness after treatment with 2% CBD + pinosylvin.

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