



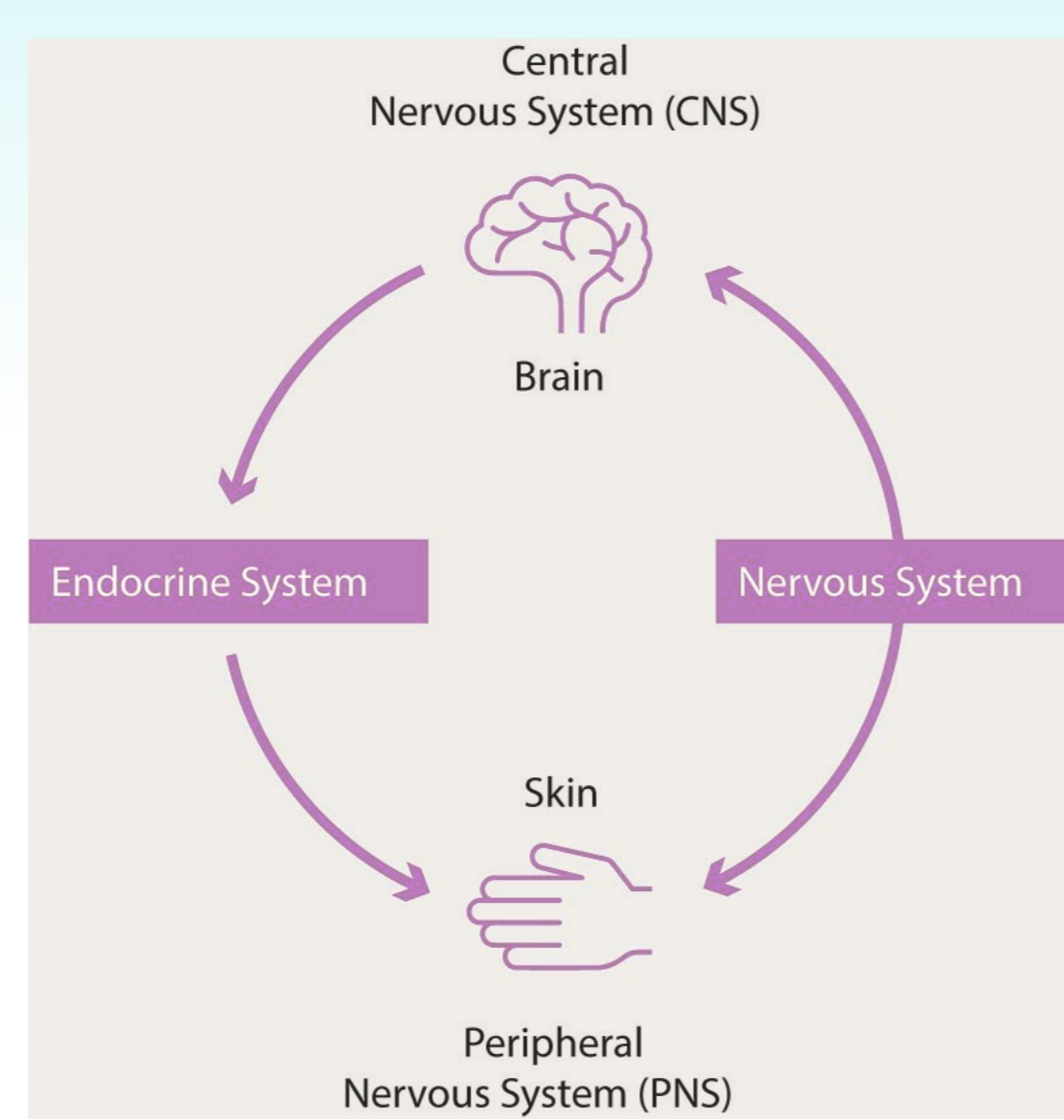
A healthy and relaxed look: Improved skin complexion and emotional wellbeing by Timut pepper extract

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Introduction

New strategies like a focus on self-care and wellness in beauty help people to improve their mental health, which in turn leads to a better-looking skin. The connection and interplay between the brain and the skin is summarized by the concept of the skin-brain axis. On the one hand, a release of stress hormones from the brain can result in skin problems which can range from a dull look to bigger problems such as acne, psoriasis, or eczema [1]. A skin that looks and feels good, on the contrary, can improve the mood. On the other hand, there is a direct connection between the skin and the brain via sensory neurons, which are peripheral nerve cells that link the skin and the brain. Besides the reduction in skin cell proliferation, aged skin shows a natural decline of skin innervation, which may be linked to impaired skin functions and the skin-brain communication [2; 3]. In our study, we tested the effect of a timut pepper extract on the functions of neurons in the skin and its potential to support a healthy-looking skin and emotional wellbeing.



Materials & Methods

Cell cultivation and treatment

Human sensory neurons derived from hiPS cells (human induced pluripotent stem cells) were plated on 96-well plates coated by a thin layer of Matrigel in a differentiation medium. After 9 days of culture, the medium was changed to a maturation medium for sensory neurons. The next day, the medium was changed to a maturation medium containing or not 0.1 % timut pepper extract or 10 µM β-endorphin. Adult keratinocytes were amplified beforehand and then added above the sensory neurons on day 14 of culture. After 19 days of culture cells were fixed in a paraformaldehyde solution.

Neuron number, neurite length and keratinocyte proliferation

For the analysis of neurons and keratinocytes, cells were immunostained for β-tubulin and Ki67. The nuclei were stained with Hoechst's solution. Neurons were counted and the length of the neurites and the number of keratinocytes expressing Ki67 was measured for each condition. Statistical analysis was performed using a One-way ANOVA test followed by a Dunnett's test.

Clinical study on a stressed volunteer panel

A placebo-controlled, randomized, double-blind clinical study was performed on a panel of volunteers that was selected based on them feeling stressed and/or uncomfortable in their skin, which was assessed via a questionnaire. A total of 43 female volunteers aged between 40 and 61 years were split into two groups. One group used a cream containing 2 % timut pepper extract twice daily for 28 days, whereas the other group used a corresponding placebo cream on their face. At the beginning and the end of the study, skin complexion was assessed by a spectrophotometer at 20 different spots on either the jaw or the forehead of each volunteer. For each region, the standard deviation of the L* (lightness) or b* (blue-yellow) values was calculated as a measure of skin tone evenness between the different spots.

Testing emotional wellbeing with a neuropsychological test

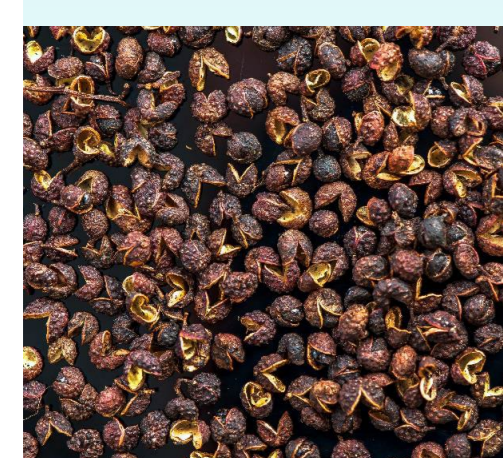
The same volunteers also performed a neuropsychological test (EmoCompass) to assess their emotional wellbeing. This neuromarketing test was for the first time applied in the field of neurocosmetics. On the first day of the study, the volunteers performed the EmoCompass test twice, before and after the first application of the cream as well as after 28 days. Only volunteers who did not show extreme emotional changes during the study period were included (n=30). For the test, the volunteers were asked the question "How do you feel?", which they answered non-verbally by generating emotional patterns consisting of coded shapes and colors on a computer screen. The analysis of the emotional patterns results in intensity values for the five emotional dimensions:

- D1 – friendly, soft, pleasant
- D2 – inspired, innovative, refreshed
- D3 – powerful, energetic, dynamic
- D4 – safe, relaxed, balanced, calmed
- D5 – excellent, sophisticated, noble

Statistical analyses were performed to compare changes in these dimensions compared to initial conditions.



Conclusions

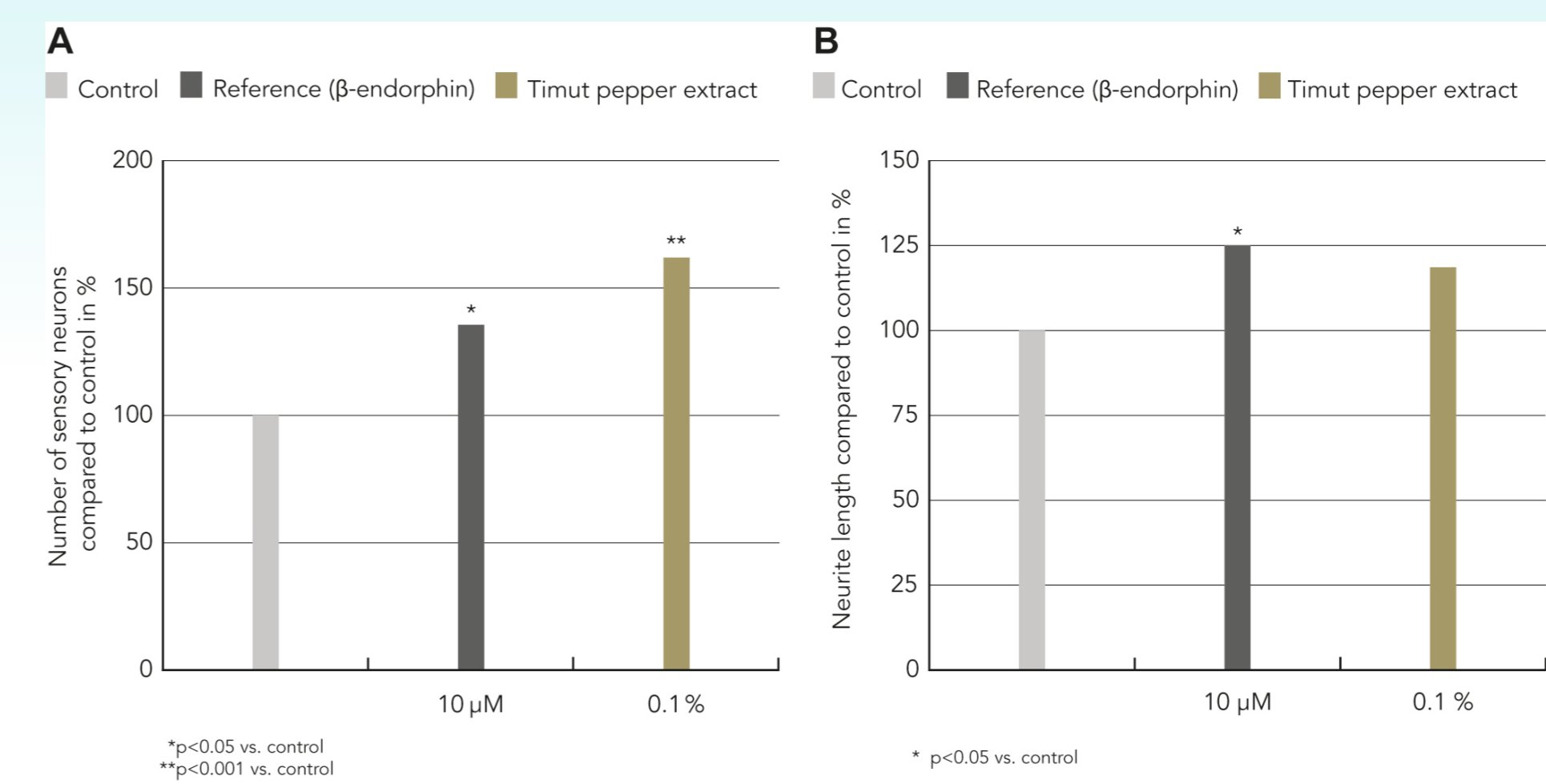


The increased focus on improving emotional wellbeing and mental health due to global concerns makes timut pepper extract a promising new development for the neurocosmetics industry. Timut pepper extract not only protects skin neurons, but also promotes a more homogeneous and healthier skin complexion and a feeling of comfort that has a positive impact on emotional wellbeing.

References

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Results & Discussion

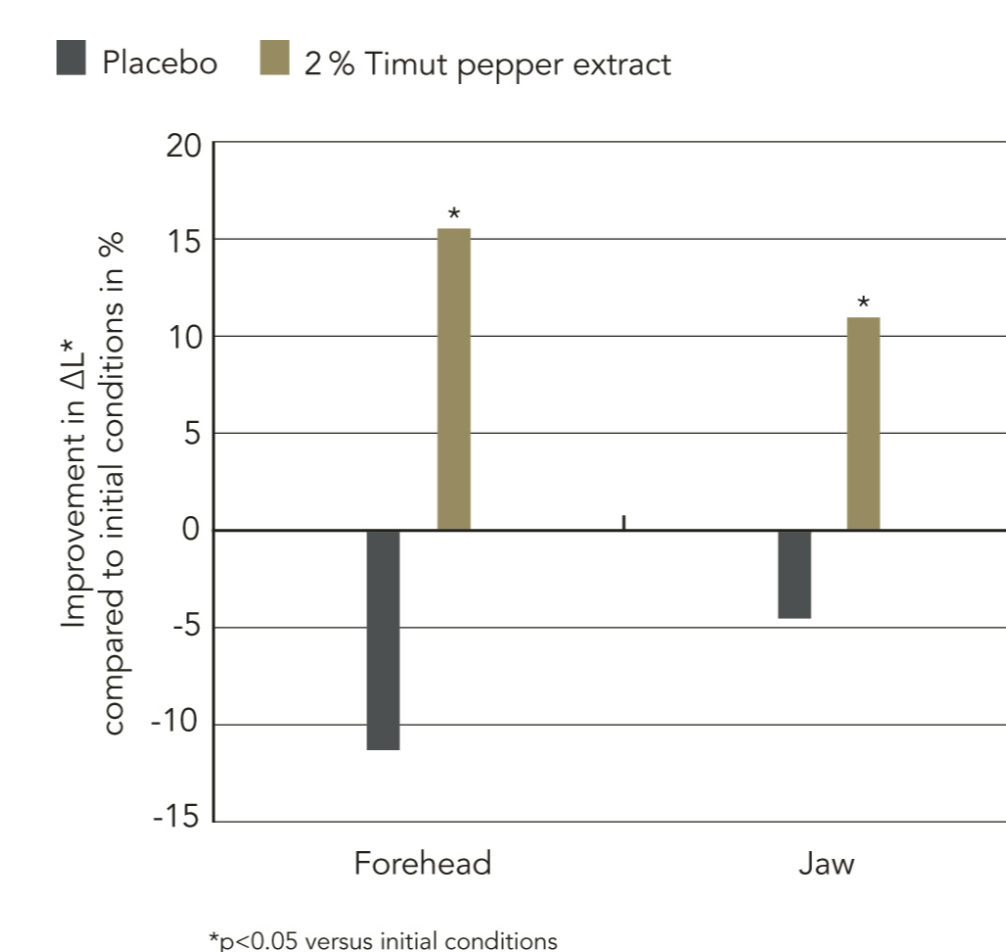
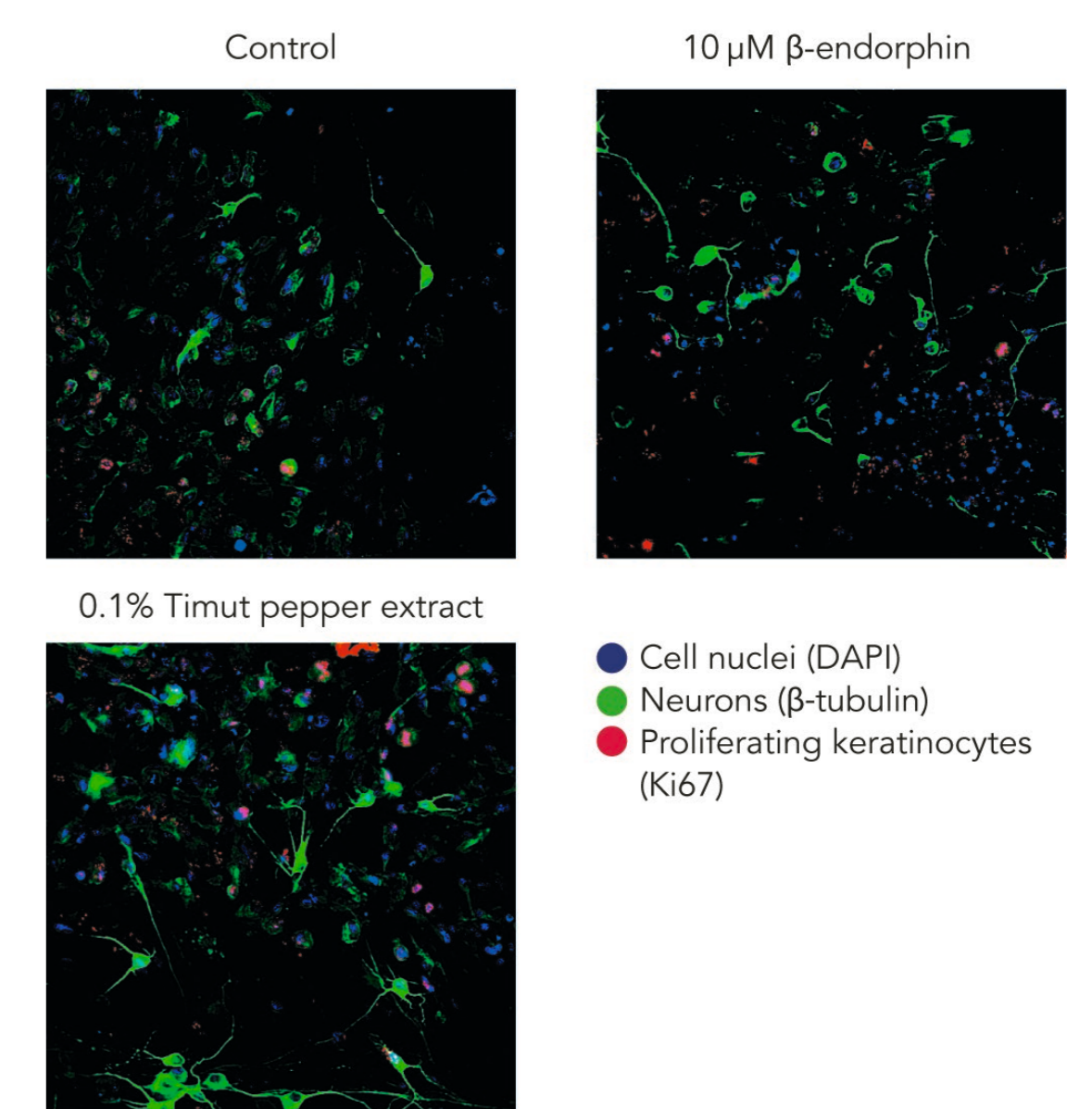


The ability of timut pepper extract to protect skin innervation was tested in a co-culture model of human sensory neurons and keratinocytes. Treatment with timut pepper extract at 0.1 % led to a significantly higher remaining number of sensory neurons (+ 62 %, Figure A) and increased neurite length (+18 %, Figure B) compared to the untreated control.

This effect was also observed in microscopy images and comparable to the effect of the reference compound β-endorphin, which is known to positively affect the number of neurons and their neurite length. Treatment with 0.1 % timut pepper extract led to an observable increase in neuron number and neurite length compared to control.

Additionally, the proliferation of keratinocytes increased significantly, resulting in a proliferation rate that was 108 % higher than that of the control.

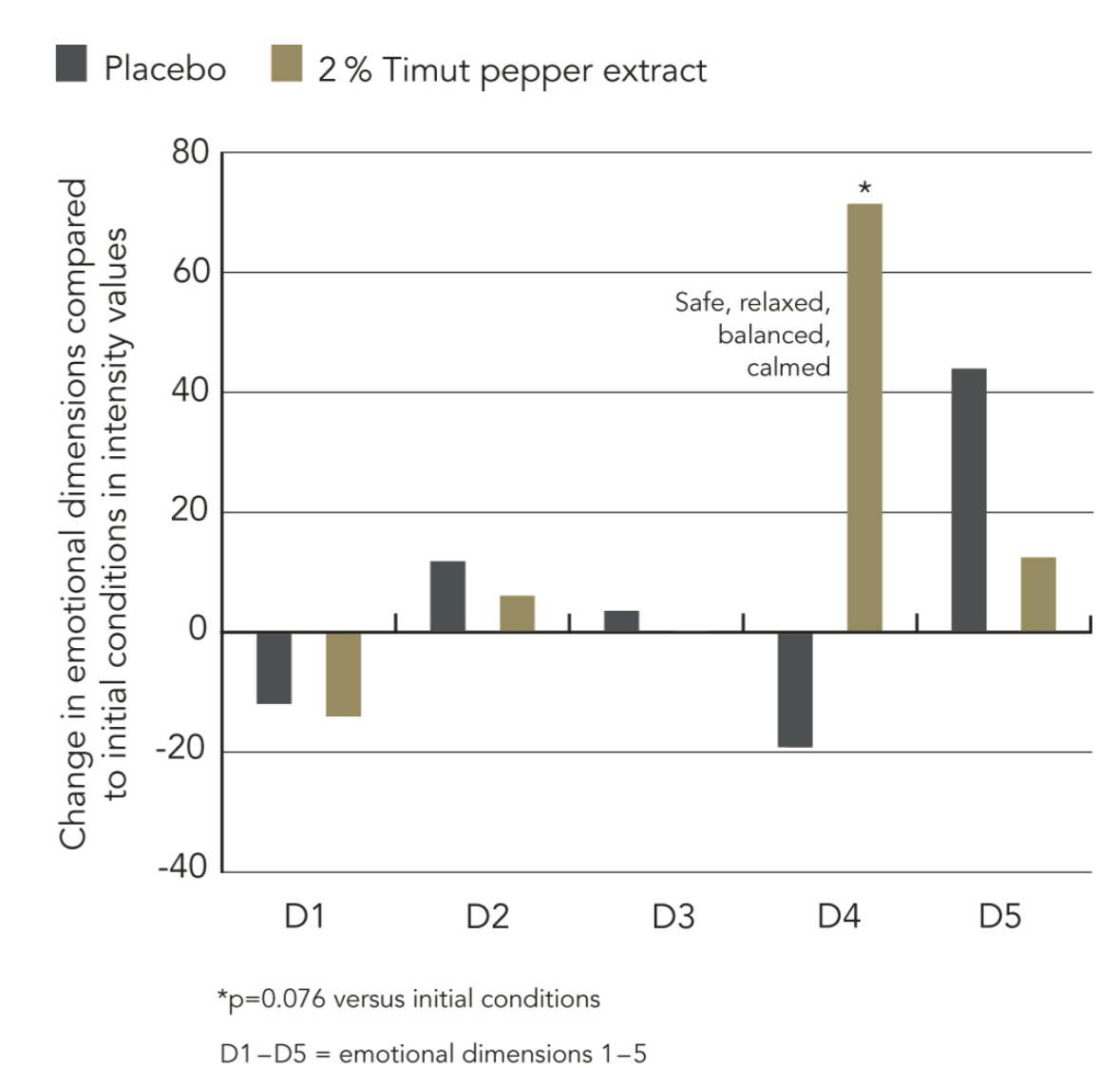
A higher number of keratinocytes can enhance the growth of neurites [4], resulting in functional and healthy skin. Considering the reduced epidermal proliferation in aged skin, by increasing keratinocyte proliferation, timut pepper extract may also support skin rejuvenation by preventing epidermal thinning.



To assess the effect of the timut pepper extract on the skin, a clinical study on a panel of volunteers feeling stressed and/or uncomfortable in their skin was performed. The treatment with timut pepper extract resulted in a significant improvement of skin tone evenness compared to initial conditions, whereas it even slightly deteriorated in the placebo group. The standard deviation of L* values (ΔL*) decreased by 26.4 % on the forehead and by 15.5 % on the jaw compared to initial conditions and placebo. A similar effect was observed for the Δb* value (data not shown). A grading by two independent experts confirmed an increased evenness of the complexion and skin luminosity, a reduced skin redness, and a fresher and healthier complexion.

The results of the EmoCompass test showed an improvement in emotional wellbeing in terms of a less stressed and more relaxed state of the volunteers who used the cream with 2 % timut pepper extract. Dimension D4, which includes emotions such as safe, relaxed, balanced, and calmed, was markedly increased after the 28-day treatment with timut pepper extract. Overall, the results for dimension D4 were significantly improved compared to the placebo group.

The other four dimensions analyzed showed no such effect. The instant posttest, which took place 5 minutes after the first application did not result in any significant changes in emotional dimensions, confirming that the observed effect was independent of the texture and fragrance of the test product.



In addition, the volunteers filled in a questionnaire, and the result of 76% of volunteers approving the proposal of a (1) more luminous skin, (2) less dull skin, (3) skin with a more even tone was statistically significant after the treatment with timut pepper extract whereas the approval of these statements was not significant in the placebo group.

Furthermore, in the self-assessment questionnaire, which was filled in by all 43 volunteers, almost double the number of volunteers in the verum group compared to the placebo group confirmed that they were less stressed than they were at the beginning of the study and that they "feel a wave of positive energy coming from within".

