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PLUMPING THE HYPODERMIS – A NEW APPROACH TO JOYFULLY EMBRACE YOURSELF

ID 113

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ADIPOGENESIS/LIPOGENESIS

qPCR

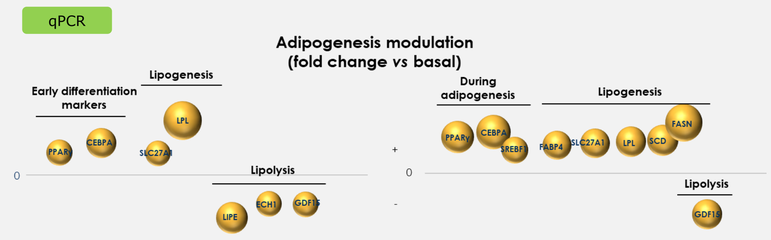


Figure 1: Lipogenesis- and adipogenesis-related gene expression during early and late terminal differentiation
(Human preadipocytes; 48 h and 7+2 d treatment with 0.2 mg/mL active ingredient; qPCR, Fig.1)

Positive effects on lipogenesis, lipolysis and adipogenesis indicated by modulation of relevant genes (e.g., upregulation of genes: SLC27A1 1.68-fold, PPARG 1.2-fold, CEBPA 2.21-fold, SREBF1 1.36-fold, FABP4 1.58-fold, SCD 1.82-fold, PPARG 1.98-fold, FASN 2.66-fold and LPL 2.69-fold, and downregulation of genes: LIPE -1.8-fold, ECH1 -1.17-fold and GDF15 -1.70-fold).

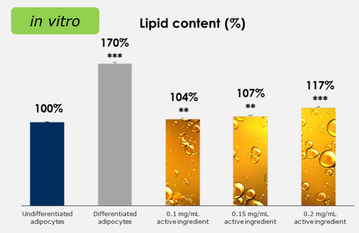


Figure 2: Improvement of lipid content
(Human preadipocytes; 7+2 d with 0.1, 0.15 and 0.2 mg/mL active ingredient; AdipoRed™, fluorescence λ=520 nm, Fig.2)

Positive effects on differentiation, but also on accumulation of lipid content (lipid content by 17%, Fig.2, and perilipin by 33%, Fig.3) in adipocytes, that is essential for a macroscopic plumping effect.

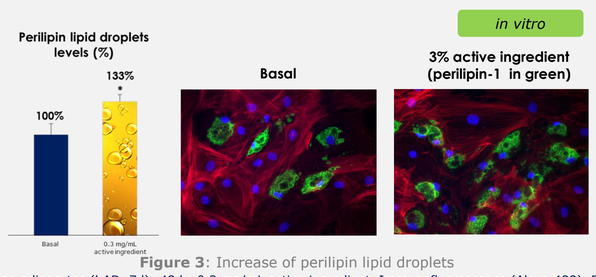


Figure 3: Increase of perilipin lipid droplets
(Human adipocytes (hAD, 7d); 48 h; 0.3 mg/mL active ingredient, Immunofluorescence (Alexa 488), Fig.3)

ECM

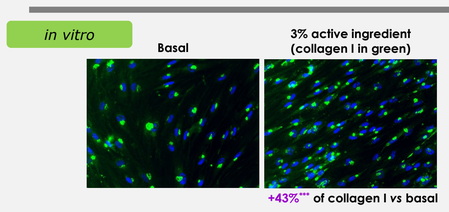


Figure 4: Increase of Collagen I
(Human Dermal Fibroblast adult (HDFa) treated with supernatant co-culture (HDFa + hAD); 4 d; Immunofluorescence (Alexa 488), Fig.4)

A novelty of the active ingredient's action is the improvement in communication between the hypodermis, mainly adipocytes, and the dermis/adjacent fibroblasts. We found that adiponectin released mainly by adipocytes after treatment with the active ingredient triggered the production of collagen (collagen I by 43%) in adjacent fibroblasts.

ANTI-OXIDANT/ANTI-INFLAMMATION

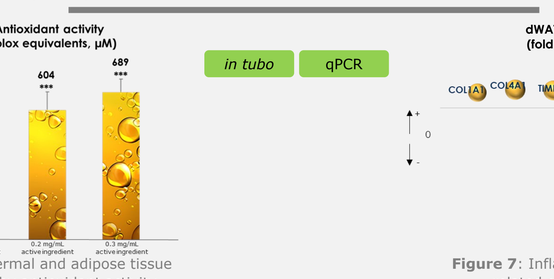


Figure 5: Improvement of anti-inflammatory and pro-inflammatory cytokines
(Co-culture: Human Dermal Fibroblast, adult (HDFa) and differentiated adipocytes; 24 h with 0.1, 0.2 and 0.3 mg/mL active ingredient; ELISA, Fig.5)

The active ingredient can improve inflammaging in dWAT by lowering pro-inflammatory cytokines (IL-8 by -66%) and increasing anti-inflammatory factors (adiponectin by 22%).

Figure 6: Dermal and adipose tissue protection by antioxidant activity
(in tubo; 0.1, 0.2 and 0.3 mg/mL active ingredient; Trolox Equivalent Antioxidant Capacity TEAC, Fig.6)

Due to its high antioxidant molecule content, the antioxidant activity of the active ingredient (689 µM Trolox equivalents) could be confirmed as expected.

in tubo | qPCR

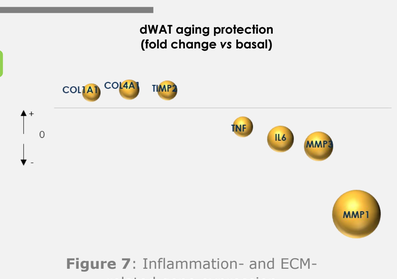
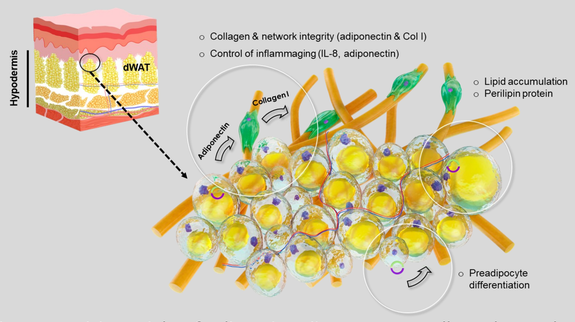


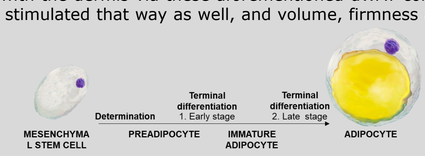
Figure 7: Inflammation- and ECM-related gene expression
(Human preadipocytes; 47+2 d treatment with 0.2 mg/mL active ingredient; qPCR, Fig.7)

Positive effects on inflammation- and ECM-related gene expression (e.g., upregulation of genes: COL1A1 1.23-fold, COL4A1 1.47-fold, TIMP2 1.42-fold, and downregulation of genes: IL6 -1.56-fold, MMP1 -8.68-fold, MMP3 -2.57-fold and TNFa -1.19-fold)

BIOLOGICAL BACKGROUND



Adipose tissue consists mainly of adipocytes, its precursor cells and vascular endothelial cells, which are embedded in connecting tissue consisting of collagens and other extracellular matrix components that serve as a scaffold for these cells.[1,2] Similar to damage caused by extrinsic and intrinsic factors in the epidermis and dermis, also the hypodermis suffers from these factors.[3] These events lead to a replacement of healthy dermal white adipose tissue (dWAT) by inflamed fibrotic structures that macroscopically presents itself as a sunken, saggy face partly due to unfavorable relocation of facial fat and weakened structures.[3,4] Even, e.g., UV light can influence the hypodermis by penetrating the skin deep enough to reach the tips of dWAT columns. However, since the hypodermis can communicate with the dermis via these aforementioned dWAT columns, the production of collagen can be stimulated that way as well, and volume, firmness and inflammation can be improved.[2,5,6]



ORIGIN

The active ingredient is a unique blend of *Vitis vinifera* and Black Cohosh extracts, and possesses the ability to counteract previously mentioned signs of aging.

Vitis vinifera is the Latin name of the common grape vine (Monastrell grape variety from Spain), and its extract is known for the abundance of polyphenols, anthocyanins a subtype of flavonoids, and other antioxidants, which can even be enriched due to the origin of the extract, a so-called callus culture.

The root extract of Black Cohosh, which originally could be found in North America, is very rich in polyphenols and isoflavones.

CLINICAL STUDY-SKIN

20 Caucasian women
50-60 years old (menopausal range)
2x a day, split face
timepoints: 7, 14 & 28 days

***p<0.01 vs T0, *p<0.05 vs T0*
****p<0.001 vs placebo,*
***p<0.01 vs placebo*

In a clinical study, brightness (significant increase in radiance by 25.2%), erythema (significant decrease of -7.8%), wrinkles in the crow's feet (significant reduction by -10.7%) and nasolabial fold (significant reduction by -6.3%), and a plumping effect on the cheekbones (significant increase of 0.52 mm in the measurement along the curvature of the cheekbones) were assessed.

Figure 8: Crow's feet wrinkle volume
(28 d treatment with a formulation containing 3% of active ingredient; PRIMOS 3D; Fig.8)

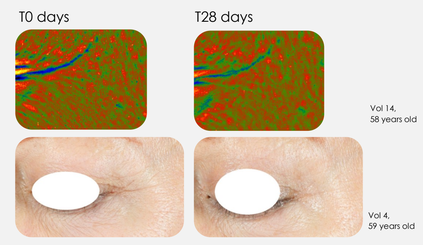


Figure 9: Crow's feet wrinkle volume
(28 d treatment with a formulation containing 3% of active ingredient; Visia®-CR & PRIMOS 3D images; Fig.9)

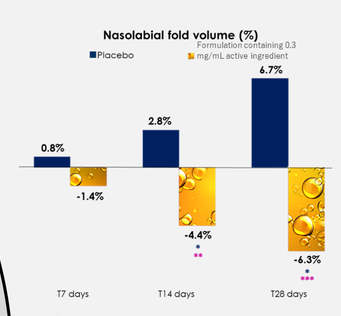


Figure 10: Nasolabial fold volume
(28 d treatment with a formulation containing 3% of active ingredient; PRIMOS 3D; Fig.10)

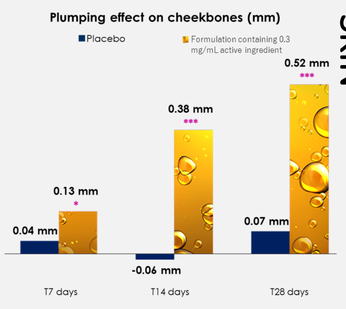


Figure 11: Plumping effect on cheekbones
(28 d treatment with a formulation containing 3% of active ingredient; PRIMOS 3D; Fig.11)

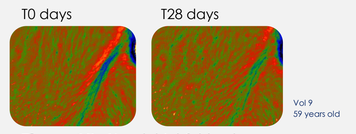


Figure 12: Nasolabial fold volume
(28 d treatment with a formulation containing 3% of active ingredient; PRIMOS 3D images; Fig.12)

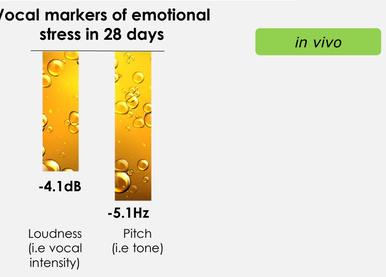


Figure 13: Vocal markers of emotional stress
(28 d treatment with with a formulation containing 3% of active ingredient; were loudness (i.e. vocal intensity) represented by the mean amplitude measured in dB and pitch (i.e. tone) represented by the mean fundamental frequency measured in Hz; Fig.13)

For a normal human being changes of vocal markers of emotional stress are usually only receivable on a subconscious level, but experts can interpret the change in loudness and pitch, and assign them to an emotional stress level. Loudness could be reduced by -4.1 dB and the vocal pitch could be lowered by -5.1 Hz.

10 Caucasian women
50-60 years old (menopausal range)
2x a day, whole face
timepoint: 28 days
✓ Vocal analysis
✓ Projective test

in vivo

Figure 14: MOOD improvement in 28 days
(28 d treatment with a formulation containing 3% of active ingredient; Projective test: a trio of different images were presented to the volunteers 15 times. They must chose one of the three for each trio at each time. The trio had three emotional dimension; Fig.14)

A projective test revealed that balance (positive passive) could be improved by 7.1%, dynamism (positive active) by 6.5%, and negative emotions could be decreased by 50%. Improvement in skin appearance seems to have a satisfying emotional effect on the consumer, which can be evaluated by the parameters measured.

Conclusion

The active ingredient induces adipogenesis, lipid accumulation and prevents the adipose tissue aging by modulating its inflammation and increasing the collagen I content in the hypodermis due to the communication between adipocytes and fibroblasts. The active is able to reduce crow's feet and nasolabial wrinkles as a plumper ingredient, soothes erythema and brings radiance to the skin. Also, it increases the positive mood and decreases the vocal markers of stress. These results underline the long-term potential of our product enhancing the mood of people in addition to its general anti-aging benefits.

References

1) Wollina U, Wetzker R, Abdel-Naser MB, Kruglikov IL. Role of adipose tissue in facial aging. Clin Interv Aging. 2017;12:2069-2076.

2) Kruglikov I, Trujillo O, Kristen Q, Isac K, Zorko J, Fam M, Okonkwo K, Mian A, Thanh H, Koban K, Sclafani AP, Steinke H, Cotofana S. The Facial Adipose Tissue: A Revision. Facial Plast Surg. 2016 Dec;32(6):671-682.

3) Kruglikov IL, Scherer PE. Skin aging: are adipocytes the next target?. Aging (Albany NY). 2016;8(7):1457-1469.

4) Ejaz A, Hatzmann FM, Hammerle S, et al. Fibroblast feeder layer supports adipogenic differentiation of human adipose stromal/progenitor cells. Adipocyte. 2019;8(1):178-189.

5) Gregoire FM, Smas CM, Sul HS. Understanding adipocyte differentiation. Physiol Rev. 1998 Jul;78(3):783-809.

6) Ouchi N, Walsh K. Adiponectin as an anti-inflammatory factor. Clin Chim Acta. 2007 May 1;380(1-2):24-30.