ACTIVE SUBSTANCES OF EDELWEISS FOR SKIN HEALTH: FROM MOLECULAR MECHANISMS TO FUNCTIONAL COSMETICS

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Aim of the study: Edelweiss (*Leontopodium alpinum Cass*.) is traditionally employed in folk medicine and cosmetology to protect skin from photo-damage and premature ageing, to accelerate wound healing and attenuate chronic cutaneous inflammation. In nature, the plant is sparsely presented, therefore industrial production of callus cultures of Edelweiss was established. The major goals of the study were to determine biologically active substances in the *Leontopodium alpinum Cass.* callus cultures having beneficial effects towards human skin cells. Molecular mechanisms leading to skin cell photo-protection, anti-inflammatory, wound healing, and anti-ageing effects were evaluated in order to provide a background for the development of cosmetic compositions containing Edelweiss isolated actives or plant extracts.

Cell Cultures and Methods applied: *Callus cultures* were established by stimulation of Edelweiss flower meristem cells and elicitation of phenylpropanoid biosynthesis. Homogenates of callus cultures (ECC) were extracted by methanol, analysed by HPLC-ESI-MS, and concentrated under reduced pressure until the concentration of the total phenolic fraction reached 55% (ECC55) and levels of leontopodic acids (LA-A and LA-B) were 3%. ECC55 and isolated LAs were studied for their anti-inflammatory properties in *primary human keratinocytes* (PHK), *fibroblasts*, and *endothelial cells* (HUVEC). Inflammatory responses were induced by UV radiation (UVC or UVA or solar simulating UVA+UVB), lipopolysaccharide (LPS), oxidised low density lipoprotein (oxLDL), and mixture of pro-inflammatory cytokines. Trichostatin A, a sirtuin inhibitor, was used to induce cultured keratinocyte senescence. Wound accelerating effects of LAs were studied in the *in vitro* keratinocyte model. Broad band UV protecting properties were determined by spectrophotometry and cytotoxicity test (using HaCaT, PHK, and fibroblasts).

Statistical evaluation: Data analysis was carried out with the software for Windows XP. Results were expressed as the mean±SD. To evaluate the difference between experimental groups, Student's t-test was applied and P values < 0.05 were considered to be significant.

Results: ECC55 (10-50µg/mL) protected PHK, HaCaT, and fibroblasts from solar UV-induced damage by enhancing early intracellular levels of nitric oxide although UV-induced expression of inflammatory genes did not read yet. LAs define very high UVC, UVB (SPF), and stable UVA protection of cultivated skin cells mainly due to a broad band UV absorption and low photo-destruction and photo-toxicity of metabolites. Comparison of dose-dependent inhibition of the chemokine *de novo* synthesis by PHK activated by TNFα+IFNγ showed that LAs were mainly responsible for the anti-inflammatory effects of ECC55. Both ECC55 and LAs were as effective as classical synthetic steroid anti-inflammatory drug Triamcinolone. Markers of cell cycle, proliferation, and apoptosis affected by SIRT inhibition, were restored by ECC55 (anti-senescence effect). The extract selectively inhibited LPS-induced *IL-6* and *VCAM1* as well as *VCAM1* induced by oxLDL in HUVEC.

Conclusions: The results obtained allowed to develop and clinically test functional cosmetics (serums) containing alcohol extracts of *Leontopodium alpinus Cass*. callus cultures.