DIFFERENTIAL MODULATION OF STRESS-INFLAMMATION RESPONSES BY PLANT POLYPHENOLS IN CULTURED NORMAL HUMAN KERATINOCYTES AND IMMORTALIZED HACAT CELLS

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Environmental and endogenous stresses to skin are considered causative reasons for skin cancers, premature ageing, and chronic inflammation. Screening of substances with preventive and/or curative properties is currently based on mechanistic studies of their effects towards stress-induced responses in skin cell cultures.

We compared effects of plant polyphenols (PPs) on the constitutive, UVA-, LPS-, or TNF-alpha-induced inflammatory responses in cultured normal human epidermal keratinocytes (NHEK) and immortalized HaCaT cells.

Representatives of three classes of PPs, flavonoids, stilbenoids, and phenylpropanoids were studied. Their effects on mRNA were determined by qRT-PCR; protein expression was assayed by Western blot and bioplexed ELISA; phosphorylation of Akt1, ERK1/2, EGFR, and NF\kappa B was quantified by intracellular ELISA or Western blot.

PPs or their combination with UVA or LPS induced strong up-regulation of stress responses in HaCaT but not in NHEK. In addition, compared to NHEK, HaCaT responded to TNF-alpha with higher synthesis of MCP-1, IP-10 and IL-8, concomitant with stronger NF\kappa B activation. PPs down-regulated the chemokine release from both cell types, although with distinct effects on NF\kappa B, Akt1, ERK, and EGFR activation. Conclusion: Results of pharmacological screenings obtained by using HaCaT should be cautiously considered while extending them to primary keratinocytes from human epidermis.