

## **AFFECTING CUTANEOUS NRF2-KEAP1 PATHWAY BY UNIQUE EXOGENOUS AND ENDOGENOUS ACTIVATORS**

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The human skin, being our outermost protective barrier, sustains continuous contact with the environment. As such, its cells must be kept in a state of constant alert against external increased oxidative stress and massive environmental insults (e.g. sunlight and UV radiation, air pollution, and mechanical stress). All these insults ultimately result in an impaired redox balance and increased cellular oxidation. One of the pivotal oxidation regulation mechanisms in the skin is the Nrf2–Keap1 pathway, and its activity leads to cutaneous redox maintenance which evidently sustains the principle of hormesis. We suggest that moderate environmental stressors and skin microbiome can provide the necessary continuous stimuli for the activation of the Nrf2 pathway. We also suggest that endogenous neurotransmitters play a major role in this activation.