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Induction of antioxidant defenses by diterpenic phenolics in human fibroblasts: relevance for ageing interventions

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Abstract:
Ageing is characterised by the progressive accumulation of molecular damage, which leads to altered cellular functioning, reduced stress tolerance and susceptibility to diseases. Consumption of fruits, vegetables and herbs has been related with health promotion due to their content in bioactive phytochemicals, which can be used for ageing interventions [1]. In the present work, the ability of the phenolic diterpenes carnosic acid (CA) and carnosol (CS) to induce intracellular antioxidant defenses in normal human skin fibroblasts was evaluated, and that related with anti-ageing effects. We observed that both CA and CS, at non-toxic concentrations, induced significantly the levels of the intracellular antioxidant glutathione as well as the mRNA and protein levels of several cytoprotective enzymes, such as HO-1, ferritin, NQO1, GST and GCL. These effects seem to be redox and Nrf2 signaling dependent, suggesting that these compounds work as hormetins. The induction of these antioxidant defenses by pre-incubation with CA or CS afforded a cytoprotective action to a following oxidant challenge with tert-butyl hydroperoxide. In a physiological assay, these compounds also induced the in vitro capacity of fibroblasts to increase wound healing. In addition, pre-incubation with these diterpenic phenolics significantly protected against H$_2$O$_2$-induced premature senescence, as shown by reduced β-gal staining and high number of viable cells. In conclusion, the induction of antioxidant defenses in human skin fibroblasts by CA and CS suggests their possible use in nutritional applications toward cytoprotective and healthy ageing interventions.

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