

PROTECTIVE ACTIVITY OF CYANIDIN-3-*o*-b**-GLUCOPYRANOSIDE ON UVB CELL DAMAGE IN HUMAN KERATINOCYTES**

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Skin cancer (melanoma and non-melanoma) is by far the most common type of cancer, with a tremendous impact on morbidity, health and healthcare economics. The development of chemopreventive strategies for skin cancer is thus a high public health priority. The most important risk factor in development of non-melanoma skin cancer is chronic exposure to the UV radiation in sunlight.

UV radiation acts as a complete carcinogen in skin tumorigenesis models. UV exposure to normal skin can result in the formation of DNA thymine dimers that may lead to fixed mutations following two rounds of DNA replication. Promotion of these initiated cells to a pre-neoplastic state (KIN) may take 10 or more years, but progression to carcinoma *in situ* (with the potential for malignant conversion) may occur in one year or less. Thus, the best opportunity for intervention with chemopreventive agents is during the promotion phase.

In recent years, naturally occurring compounds present in the common diet and beverages consumed by the human population have gained considerable attention as chemopreventive agents against many cancers including skin cancers. Many studies have shown the efficacy of naturally occurring botanical antioxidants such as green tea polyphenol, silymarin, curcumin, apigenin and resveratrol against UV radiation-induced inflammation and cancer. Anthocyanins are a group of naturally occurring phenolic compounds responsible for the colour (blue, purple and red colour) of many plants, flowers and fruit. Recent studies showed that Cyanidin-3-*o*- β -glucopyranoside (C-3-G), the main anthocyanin present in juice of pigmented oranges, has a potential antioxidant activity.

In this study we investigated the cytoprotective effects of C-3-G against UVB cell damage in a cultured cell line of immortalized human keratinocytes (HaCaT). Apoptosis induction by UVB (40 mJ/cm²) is seen as an experimental model for "sunburn cell" (SBC) formation. In fact SBC formation in the epidermis is a characteristic consequence of UV radiation exposure and SBC have been identified morphologically and biologically as keratinocytes undergoing apoptosis. An experimental approach using a synthetic caspase 3 substrate and a photometric enzyme immunoassay has been used to determine the activation of caspase 3 and fragmentations of DNA evoked by exposure of HaCaT cells to UVB. Co-treatment of HaCaT cells with 12.5-100 μ g/ml C-3-G showed a dose-dependent inhibitory effect on apoptosis induced by UVB; pre-treatment with C-3-G had no cytoprotective effects. The results also demonstrated that similar concentrations of C-3-G efficiently inhibit activation of enzyme caspase 3. The maximum inhibition of apoptosis (67%) and caspase 3 (39%) was observed with 100 μ g/ml C-3-G.

These data suggest that C-3-G directly interferes with UVB; the exact mechanism of preventing UV penetration into the skin is not established, but appears that C-3-G absorbs some low wavelengths of UV spectrum (280 nm). These preliminary results support further research aimed at identifying C-3-G as a novel type of agent in photoprotection of the skin.