PREVENTIVE ROLE OF CAFFEIC ACID ON ULTRAVIOLET-B RADIATION INDUCED PHOTOCARCINOGENESIS IN SWISS ALBINO MICE

Executive Summary of Major Research Project

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In the present study, we investigated the photochemopreventive effect of caffeic acid (CA) in acute and chronic UVB radiation (280 - 320 nm) exposed Swiss albino mice. We examined whether CA can ameliorate the cellular and molecular changes during short-term UVB exposure in mice skin. We observed that CA prevents UVB-mediated loss of antioxidants status in the mouse skin. Additionally, we found that CA inhibits the activation of UVB mediated inflammatory markers (TNF-α, IL-6, COX-2 and NF-kB). In chronic studies, mice were exposed to 180 mJ/cm^2 of UVB thrice weekly for 30 weeks. The protective effect of CA was evident in terms of significant reduction in tumor incidence and tumor multiplicity in the dose of 15 mg/kg. b.wt. Histopathological observation illustrates that CA treatment decreased hyperplasia, atypical tumor cells, dysplasia and keratinous pearls as well as squamous cell carcinoma.

We also found that CA inhibits JAK-STAT3 signaling, thereby induces apoptotic cell death by upregulating Bax, cytochrome-C, caspase-9 and caspase-3 expression in UVB exposed mouse skin. Further, CA significantly prevents mRNA expression of MMP-1, MMP-2 and MMP-9 in chronic UVB exposed mouse skin. Moreover, CA treatment significantly brought down UVB-mediated expression of of iNOS, VEGF and TGF-β through activation of peroxisome proliferator-activated receptors (PPAR-γ). It has also been noticed that CA prevents UVB-induced expression of PI3K/AKT kinases through activation of PTEN which subsequently promotes XPC dependant NER proteins such as XPC, XPE, TFIIH (p44) and ERCC1. It is noteworthy that both topical and intraperitoneal treatment of CA reduces tumors incidence in chronic UVB-exposed mouse skin. All together, the present findings suggest that CA is a promising natural phytoconsitutent against photocarcinogenesis.