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Title

The potential of folate derivatives and Hantzsch esters to inhibit ultraviolet-induced reactive oxygen species

Priority 1 (Research Category)

Cancer research (not screening)

Presenters

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Abstract

Context: Ultraviolet (UV) radiation causes 60,000 premature deaths worldwide per year. In the US alone, UV-associated skin cancers cost over $8 billion annually. UV radiation causes harm primarily through inducing carcinogenic reactive oxygen species (ROS). Agents that reduce UV-induced ROS before carcinogenesis can occur are therefore highly desirable. Folate derivatives and Hantzsch esters have been shown to inhibit chemically-induced ROS, but have not been demonstrated to be effective at inhibiting UV-induced ROS. Objectives: (1) To evaluate in vitro inhibition of UV-induced ROS with a folate derivative. (2) To identify promising Hantzsch esters for further study by evaluating their energy favorability to inhibit some ROS through high precision quantum chemical methods (CBS-QB3, SMD solvent model, water). Study Design and Analysis: UACC 903 cells (Melanoma cell line) and fibroblast cells were cultured and marked with a fluorescent ROS dye. Cells were exposed to varying concentrations of a folate derivative, and ROS were induced by H2O2 or ultraviolet radiation. ROS inhibition was measured over time, and modeled on an S-shaped curve. High precision chemical methods (CBS-QB3, SMD solvent model, water) of elementary reaction steps involving the transfer of electrons (SET step), the transfer of hydrogen radicals and the transfer of hydride anions were used to evaluate the energy favorability of Hantzsch esters as ROS inhibitors and identify promising Hantzsch esters for future in vitro evaluation. Setting: In vitro analysis and quantum calculation. Intervention: Exposure to UV radiation. Outcome Measures: (1) ROS inhibition (2) Net energy of Hantzsch ester ROS interaction. Results: Folate derivatives inhibit ultraviolet radiation-induced ROS in melanoma and fibroblast cell lines in vitro. Several Hantzsch esters demonstrate energy favorability in inhibiting ROS in silico. Conclusions: Folate derivatives and their chemical analogs, Hantzsch esters, offer a method of inhibiting ROS induced by ultraviolet radiation, and hence, a potential method for reducing the tremendous health burden of ultraviolet radiation. Further study is needed to determine the extent to which this ROS inhibition decreased carcinogenesis.