DNA–PROTEIN CROSS-LINKS PRODUCED BY VARIOUS CHEMICALS IN CULTURED HUMAN LYMPHOMA CELLS

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Chemicals such as cis-platinum, formaldehyde, chromate, copper, and certain arsenic compounds have been shown to produce DNA–protein cross-links in human in vitro cell systems at high doses, such as those in the cytotoxic range. Thus far there have only been a limited number of other chemicals evaluated for their ability to produce cross-links. The purpose of the work described here was to evaluate whether select industrial chemicals can form DNA–protein cross-links in human cells in vitro. We evaluated acetaldehyde, acrolein, diepoxybutane, paraformaldehyde, 2-furaldehyde, propionaldehyde, chloroacetaldehyde, sodium arsenite, and a deodorant tablet [Mega Blue; hazardous component listed as tris(hydroxymethyl)nitromethane]. Short- and long-term cytotoxicity was evaluated and used to select appropriate doses for in vitro testing. DNA–protein cross-linking was evaluated at no fewer than three doses and two cell lysate washing temperatures (45 and 65°C) in Epstein–Barr virus (EBV) human Burkitt's lymphoma cells. The two washing temperatures were used to assess the heat stability of the DNA–protein cross-link. 2-Furaldehyde, acetaldehyde, and propionaldehyde produced statistically significant increases in DNA–protein cross-links at washing temperatures of 45°C, but not 65°C, and at or above concentrations of 5, 17.5, and 75 mM, respectively. Acrolein, diepoxybutane, paraformaldehyde, and Mega Blue produced statistically significant increases in DNA–protein cross-links washed at 45 and 65°C at or above concentrations of 0.15 mM, 12.5 mM, 0.003%, and 0.1%, respectively. Sodium arsenite and chloroacetaldehyde did not produce significantly increased DNA–protein cross-links at either temperature nor at any dose tested. Excluding paraformaldehyde and 2-furaldehyde treatments, significant increases in DNA–protein cross-links were observed only at doses that resulted in complete cell death within 4 d following dosing. This work demonstrates that DNA–protein cross-links can be formed in vitro following exposure to a variety of industrial compounds and that most cross-links are formed at cytotoxic concentrations.

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