Metal Oxo Reactions with Alkylating Agents: Implications for Cancer Prevention

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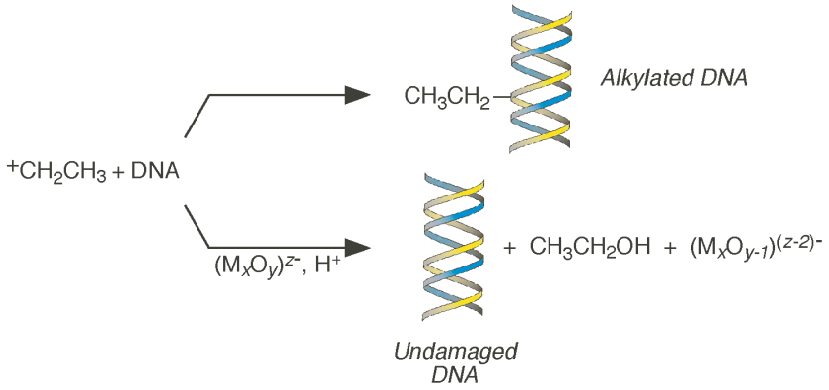
Toxins such as nitrosamines and polycyclic aromatic hydrocarbons are found in cooked foods and tobacco smoke. The toxic nature of these compounds is a result of metabolic activation to potent alkylating agents and subsequent reactions with nucleophilic positions on DNA. Also present in the human diet are a variety of inorganic compounds, many of which form anionic oxo species in water. Numerous studies involving both rats and human subjects report decreased incidences of cancer when diets are supplemented with inorganics such as selenium[1] and vanadium[2,3] salts. We hypothesize that these inorganic oxo species may be nucleophilic, reacting directly with the electrophilic alkylating toxins. By consuming the alkylating toxin prior to reaction with DNA, formation of mutagenic lesions may be prevented. We are examining the interactions of vanadium, selenium, other oxo complexes with alkylating toxins. DNA alkylation studies in the presence of such inorganics assess the direct abilities to prevent DNA damage. Here, we present results showing that simple inorganic oxo compounds both prevent DNA damage and detoxify alkylating agents by bringing about transformation to relatively harmless alcohols.[4]



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