The Role of Metal Coordination in Selenium Antioxidant Activity

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In the presence of hydrogen peroxide, iron(II) catalyzes the formation of hydroxyl radicals that damage proteins, lipids, and DNA *in vivo*. Because positively-charged metal ions in a cell localize near negatively-charged DNA, the generated hydroxyl radicals cause DNA damage. Cell death and mutation caused by DNA damage have been implicated in many conditions including cancer, neurodegenerative diseases, and aging. As a result, much work has been done to develop antioxidant treatment strategies, and selenium compounds are of particular interest due to their excellent antioxidant properties.

Current mechanisms for selenium antioxidant activity do not take into account the possibility that selenium may coordinate to iron and prevent the formation of hydroxyl radical, or neutralize it immediately after generation. To examine the role of metal coordination on the antioxidant activity of selenium compounds, plasmid DNA was treated with selenium compounds, iron(II), and hydrogen peroxide, and the resulting DNA damage was quantified using gel electrophoresis. Under these conditions, selenocystine completely inhibited oxidative DNA damage at low micromolar concentrations, whereas selenomethionine inhibited less than 50 % of oxidative DNA damage at twenty times these concentrations. UV-vis and additional gel electrophoresis experiments indicate that binding of the selenium compounds to iron is required for maximal antioxidant activity. Specific functional groups and oxidation states that affect selenium antioxidant activity will be discussed.