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A high proportion of human cancers are attributable to environmental agents including the dietary sources of mutagens and carcinogens. Several well defined classes of genotoxic compounds have been identified in processed and unprocessed foods. These include flavonoids, polycyclic aromatic hydrocarbons, safrole, furans and tannins. Therefore, dietary mutagens have attracted considerable interest and a number of studies on dietary practices in relation to cancer have been undertaken. For example, the predominance of certain foods in some countries has been related to the incidence of certain types of cancer in their populations.

Flavonoids are widely distributed plant derived dietary constituents and are genotoxic agents. They form active constituents of a number of herbal and traditional medicines. In addition to their putative environmental and dietary hazard, flavonoids have been implicated as novel antiviral and antitumor compounds. In earlier reports from this laboratory it was shown that quercetin and other flavonoids cause strand scission in DNA in the presence of Cu(II) and that this reaction is associated with the transient reduction of Cu(II) to Cu(I) and the generation of active oxygen species.

The experiments described in this thesis explore flavonoid-Cu(II) mediated DNA strand scission reactions with a variety of flavonoids differing in their hydroxyl group substitution pattern. A synthetic flavonoid (7,8 dihydroxy-flavone) that lacks the possibility of forming a complex is also examined by comparing with the reactivities of other flavonoids. Generalizations for the correlation of structure and activity are drawn and
evidence for three different modes of action of flavonoids as genotoxic agents is presented.

Previous studies by others have shown that thiols such as glutathione cause cleavage of DNA in the presence of Cu(II) ions and that the hydroxyl radical derived from molecular oxygen is the major cleaving species. I have used flavonoid quercetin as an electron donor to demonstrate that oxygen is not required for degradation of DNA by glutathione and Cu(II). Indirect evidence is presented to indicate that glutathione may substitute oxygen as an electron acceptor. In addition, DNA degradation to a significant extent occurs under anaerobic conditions and no inhibition of single-strand cleavage of supercoiled plasmid DNA is seen in the presence of superoxide dismutase and catalase. In view of the ubiquitous presence of glutathione, these results could be of interest under certain diseased conditions where copper concentrations are elevated in tissues.