SUMMARY

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 nitrosoamines, flavonoids, safrols, polycyclic aromatic hydrocarbons, pyrrolizidine alkaloids, 1,2-dicarbonyl compounds, pyrazines, pyrolysis products, 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 predominence of certain foods in some countries has been related to the incidence of certain types of cancers in their populations.

The experiments described in this thesis explore DNA damage mechanism by kojic acid and tannic acid, both of toxicological interest, as they occur in various food products. Kojic acid (5-hydroxy-2-hydroxymethyl-γ-pyrole) is a bacterial metabolic product used intensively in the food industry. In presence of visible light and molecular oxygen it was found to cause breakage of calf thymus DNA. Such degradation was considerably enhanced in the presence of transition metal ions Fe(III), Fe(II) and Cu(II). The cleavage of DNA in the presence of Fe(III) did not appear to have any preferred site(s) or sequence(s) for strand scission. Kojic acid catalyzed the reduction of transition metal which in the case of Cu(II) was found to play an essential role in the degradation of DNA. Kojic acid
also reduced oxygen to superoxide anion and hydroxyl radicals were formed in the presence of metal ions. The involvement of these active oxygen species in the reaction was established by the inhibition of DNA breakage by superoxide dismutase, catalase, iodide, mannitol, formate and sodium azide. The strand scission reaction was shown to account for the biological activity of kojic acid as assayed by bacteriophage inactivation.

Tannic acid is extracted from plant materials and has numerous industrial, pharmacological and food additive applications. DNA damage mechanism by tannic acid resembles that of kojic acid with significant contrasting features in its mode of action. It is not affected by incident light and is exclusively Cu(II)-dependent in its action on DNA. Tannic acid shows partial preference for AT sequences and involves hydroxyl radical as the proximal cleavage agent.