SUMMARY

The effect of exogenously administered chemicals vitamins C and E, β-carotene, caffeine, cysteamine and buthionine sulfoximine, against radiation-induced (1Gy) chromosomal damage was studied using whole-body irradiated mice. The end-points used for assessing *in vivo* radiobiological damage included micronucleus induction in polychromatic erythrocytes (PCEs) of bone marrow and radiation-induced block to cell-cycle progression. The chemicals were administered to the animals either orally or by intraperitoneal injection, before or after irradiation, in acute or chronic doses. Each chemical was tested over a range of concentrations and dose-response curves were generated. The major findings are as follows-

1. All chemicals, except β-carotene, afford significant radioprotection when administered 1-2 h before irradiation. Some chemicals, such as vitamins C and E and caffeine afford protection even if they are given within a few minutes **after** irradiation. Only vitamins C, and no other chemical, is effective even when administered **2 h after** irradiation.

2. β-carotene affords protection when it is given in multiple doses for a week before irradiation but does not protect when given once, before/ after irradiation. On the other hand, ascorbic acid, α-tocopherol, caffeine, cysteamine and BSO, are not effective if they are given daily, in small doses, for a week before irradiation. These observations indicate that the daily intake of these nutrients/ chemicals (with the exception of β-carotene) at the normal or increased levels, may not result in a generally enhanced radioresistance.

3. The dose-response curves for different chemicals show that for each chemical there is a 'threshold' dose below which there is no radioprotection. For most chemicals, optimal radioprotection occurs over a range of doses and does not increase linearly with dose.

4. The chemicals in increasing order of their maximum protective efficiency are as follows:

β-carotene >cysteamine > α-tocopherol >BSO >caffeine >ascorbic acid

On an equimolar basis of comparison, the sequence in increasing order is as follows -

cysteamine > α-tocopherol > caffeine > BSO > ascorbic acid

(for an acute dose of 10^{-2} M/kg)

α-tocopherol and BSO are probably the most efficient radioprotectors of bone marrow chromosomes since these afford significant protection even at concentrations as low as 10^{-3} M/kg body-weight.

5. Protection by post-irradiation treatment of chemicals has implications for both basic and applied fields. The finding that vitamins C,E and caffeine greatly reduce the radiation-induced damage when given immediately after radiation exposure, raises hopes regarding their suitability for therapeutic use in emergencies such as radiation accidents. On the other hand, the observation that radioprotection occurs even when chemicals are given after irradiation, indicate that the mechanism(s) of development of radiation-induced chromosomal damage *in vivo* are much more complex than 'breakage followed by reunion', and possibly occur over a larger time-scale (few minutes to

hours) after irradiation.

6. The finding that certain chemicals protect in post-irradiation treatments while others are effective only when present during the clastogenic exposure, indicates that different classes of chemicals intercept at different points, the sequence of events leading to the chromosomal damage. The observation that some chemicals, like β-carotene and α-tocopherol afford greater protection than others, suggests that certain steps (or intermediates) in the sequence of events may be more important than others in determining the biological consequences of radiation exposures.

7. Whereas it may be possible to explain the radioprotective effects of chemicals administered before irradiation on the basis of their ability to scavenge free-radicals generated during irradiation, it is more difficult to do so for chemicals that protect in post-treatments. Apart from the possible role of these chemicals in biochemical repair processes, there is also a possibility that post-irradiation protection by chemicals involves elimination of long-living radical(s) involving target molecules that have a stable configuration; there is now evidence that certain organic radicals (having a half-life of about one day) do persist at room temperatures in mammalian cells irradiated by γ-rays (Yoshimura *et al.* 1993).