INTRODUCTION
The demonstration of "artificially produced" mutation in Drosophila by exposure to X-rays (Muller, 1927), was followed by a series of elegant studies which eventually led to the observation of radiation-induced transmissible genetic changes in various organisms including mammals. Widespread concern over the possible catastrophic consequences of human exposure to ionizing radiation was expressed immediately after the second world war. This resulted in the compelling need to generate reliable data for predicting genetic risks to humans, originating from exposure to ionizing radiation. Today, there is a growing awareness of the importance of genetic risk assessment associated with occupational and/or environmental exposure to low levels of radiation because of the expanding nuclear power industry and the ever increasing peaceful uses of atomic energy.

The feasibility of chemical protection against radiation hazards has been known for over fifty years. During this period, much has been learned about the nature of radiation-induced injury and the factors governing the expression of that injury. The extensive
literature on chemical radio-protection suggest that thousands of compounds have been tested for radioprotective efficacy and numerous theories have been proposed to explain their actions (Livesey and Reed, 1987).

The extent of genetic and somatic alteration of cellular constituents which occur after exposure to ionizing radiation is known to be related to the status of the cellular defence systems. A number of characteristics of cellular biochemistry and physiology interact to determine natural or inherent radiosensitivity. The protection of vital cellular constituents is dependent on the structural integrity of the cell and the presence of certain endogenous radioprotective substances like glutathione and enzymes like glutathione S-transferase, epoxide hydrolase, superoxide dismutase, catalase, glutathione peroxidase and glutathione reductase (Greenstock, 1981; Livesey and Reed, 1987). Nonenzymatic reactions involving agents like ascorbic acid, alpha-tocopherols and β-carotene are also known to play an important role in cellular protection (Burton and Ingold, 1989; Willson, 1983). By manipulating some of these factors, it may be possible to increase or decrease natural radiosensitivity.
Several nutritional and environmental chemicals have found a place in the long list of agents which modulate the effects of ionizing radiation. This includes some of the minor constituents of our commonly consumed foodstuffs and beverages which are capable of exerting in vivo protective effects against genetic damage induced by ionizing radiation (Abraham, Sarma and Kesavan, 1993; Sarma and Kesavan, 1993). Hence it would be practically impossible for anyone to consume a diet devoid of naturally occurring anticlastogenic compounds because of their diversity and widespread occurrence (Ramel et al., 1986). Dietary antioxidants like ascorbic acid, alpha-tocopherol, β-carotene, chlorogenic acid, chlorophyllin and curcumin are already well known for their radioprotective properties (Abraham, Sarma, Kesavan, 1993; 1994; Sarma and Kesavan, 1993; Sarma, Abraham and Kesavan, 1994). Therefore an assessment of genetic risk arising from exposure to radiation would be more meaningful and realistic if the modulatory role of nutritional and environmental chemicals is not overlooked.

The practice of studying the effects of high doses of radiation and then extrapolating it to low doses has been questioned. Similarly, a highly relevant question is whether or not modulatory effects
observed with high doses of protective agents against relatively high doses of radiation would hold good for low doses of radioprotective chemicals and doses of radiation $<0.5\ \text{Gy}$. A recent study from this laboratory on the radioprotective effects of garlic extract which is rich in organosulphur compounds demonstrated dose-related protective effects against high doses of gamma-radiation (1 and 2 Gy) but not against low doses ($<0.5\ \text{Gy}$) (Singh, Abraham and Kesavan, 1996). This observation highlighted the need for more studies to evaluate the protective effects of low doses of radioprotective chemicals against low doses of ionizing radiation.

Cellular response to ionizing radiation can be modulated by agents which enhance/inhibit the endogenous level of glutathione, a tripeptide involved in protection. At present there are dietary agents and environmental chemicals which are known to enhance the glutathione levels in experimental animals (Wattenberg, 1982; 1985). Glutathione levels can also be decreased by treatment with chemicals like buthionine sulfoximine which inhibits gamma-glutamylcysteine synthetase (Meister, 1987; Biaglow et al., 1983; Griffith and Meister, 1979). In this context, the question to be answered is whether or not manipulation of glutathione
levels by the administration of nutritional and environmental chemicals is associated with changes in the extent of genetic damage induced by radiation.

Another aspect which would be of interest to know is how "protective" chemicals interact when they are administered in combinations and not as individual compounds. Such interactions cannot be ignored if one takes into consideration the realistic situation (Abraham, 1996). A classical example in this context is the interaction between the naturally occurring antioxidants ascorbic acid and alpha-tocopherol which suggests that alpha-tocopherol radical reacts rapidly with ascorbic acid. As a result ascorbic acid may have a "sparing effect" on alpha-tocopherol (Packer et al., 1979). Many such interactions leading to synergistic/additive/antagonistic effects can be expected when two or more nutritional and/or environmental chemicals are consumed (Abraham, 1996).

Appropriate in vivo test systems are needed to assess the modulation of the genetic effects of low doses of radiation and for elucidating the possible mechanisms involved. Test systems selected for this purpose should be suitable for evaluating the entire spectrum of genetic changes (gene mutations and chromosomal alterations) induced by radiation. Since every test
system has its limitations, this can be achieved only by using a combination of two or more test systems, which are suitable for evaluating both genetic and biochemical effects. The classical Drosophila assay for detecting sex-linked recessive lethal mutation is the best validated test which has been extensively used for investigations on the genetic effects of ionizing radiation. With respect to the genetic end point scored, the recessive lethals are heterogenous, because they comprise point mutations (forward mutations and deletions) as well as small and large rearrangements. This test is very sensitive because genes on the whole X-chromosome are tested and the X-chromosome represents about 20% of the entire genome. It has been estimated that 600 to 800 genes out of a total of approximately 1000 X-chromosome genes are assayed this way and hence the test for sex-linked recessive lethal mutations, remains as the best Drosophila assay (Würgli, 1983). The highly versatile Drosophila system can also be used to evaluate the induction of translocations (II-III autosomal translocation) and loss of X or Y chromosomes (Würgli, Sobels and Vogel, 1984). Besides Drosophila larvae are highly suited for biochemical investigations (Abraham, Singh and Kesavan, 1993). For in vivo studies on chromosomal damage, the mouse test systems are widely used. The mouse bone marrow micronucleus
test and the chromosome aberration test are among the best validated in vivo mammalian tests, which can rapidly yield valuable information on the extent of radiation-induced genetic damage with or without modulators. The present in vivo study was undertaken using Drosophila and mice.

The experimental work was divided into three parts.

**Part I** deals with: The genetic effects of tritiated water (HTO) and gamma radiation in different germ cell stages of adult male Drosophila malanogaster flies, the genetic effects of HTO and gamma-radiation in the germ cells of Drosophila larvae and modulation of genetic effects of gamma-radiation in germ cells of Drosophila larvae after pre-treatment with nutritional and environmental chemicals.

**Part II** deals with: Genetic effects in bone marrow cells (micronucleus test) after exposure to HTO and low doses of gamma radiation, modulation of the genetic effects of low doses of gamma radiation by pre-treatment with low doses of nutritional and environmental chemicals and induction of chromosome aberrations in bone marrow cells of mice by exposure to low doses of gamma radiation and its modulation by chemicals.
Part III deals with assays to: Estimate the sulphydryl content and glutathione S-transferase activity in Drosophila larvae after pre-treatment with buthionine sulfoximine, to evaluate the genetic damage in the germ cells of Drosophila larvae after decreasing the sulphydryl content and glutathione S-transferase activity, to assess the effects of pre-treatment with dietary antioxidants on the sulphydryl content and glutathione S-transferase activity in the livers of mice and to assess changes in sulphydryl content and glutathione S-transferase activity in the livers of mice after pre-treatment with chemicals which are known to be either "enhancing" or "inhibiting" agents.