Aim and Objectives
Various factors regulate cell division (Bradshaw and Prentis 1987, Cross and Dexter 1991, Sawyer et al. 1991). It has been proposed that dicarboxyls change the electronic nature of protein by binding and modifying susceptible amino acid residues leading to the arrest of cell division (Szent-Gyorgyi 1973, 1977).

Several studies have suggested the possibility of involvement of glyoxalase system in the regulation of cell division in plants and animals (Alexender and Boyer 1971, Sutrave 1979, Ramaswamy et al. 1983, Bagga et al. 1987, Sethi et al. 1988). A direct relationship between cell cycle and glyoxalase system has also been observed (Hooper et al. 1988).

It is well established that radiosensitivity is directly proportional to the rate of cell division and inversely proportional to the degree of differentiation (Arena 1971). The glyoxalase system is modulated during cell division and differentiation (Thornalley 1990), therefore, it may play an important role in cellular radiosensitivity. Moreover, glutathione is a cofactor in the glyoxalase system and an important factor determining inherent cellular radiosensitivity (Revesz et al. 1984). Many investigators (Astor et al. 1984, Louie et al. 1985, Clark et al. 1986, Vander Schans et al. 1986, Vos et al. 1986, Sauder et al. 1991) have found that depletion of intracellular GSH increased the radiosensitivity of cells. GSH depletion leads to less detoxification of radiation produced peroxyl radicals or hydroperoxides (Biaglow et al. 1984, 1986). Thus it appears that there might be some relationship between cellular damage and glyoxalase system. Therefore, in the present work an attempt was made to study the effect of γ-radiation on the glyoxalase system and its modification by chemical modifiers.


As mentioned above, several studies have suggested the possibility of involvement of glyoxalase system in the regulation of cell division in animals as well as plants. Since the glyoxalase phenotypes are among the earliest expressed in embryogenesis and persist throughout development, tissue maturation, senescence until cell death (McLellan and Thornalley 1989), modulation of its activity may occur during development and ageing.

Methylglyoxal, oxoaldehyde and S-D-lactoylglutathione are substrates for the
glyoxalase system and are toxic at higher concentration (Thornalley 1990, 1993). Methylglyoxal induces the generation of active oxygen species (Kalapos et al. 1993) and the same might be true for S-D-lactoylglutathione and α-oxoaldehydes. Accumulation of these physiological substrates may cause the generation of free radicals. It is well established that ageing results from deleterious damage to tissue by free radicals produced during metabolism.

The importance of the correlation between ageing and the alteration in the activities of regulatory enzymes, cofactors and coenzymes that are substrates or activators of diverse enzymes has been suggested (Stadtman 1988). The glyoxalase system is considered vital for biological functions like cell division, vesicle mobilization, detoxification, diabetes mellitus and cancer (Thornalley 1990). Moreover, GSH is a substrate for diverse enzymes.

Since the glyoxalase system is involved in cell growth and its substrates are toxic and GSH is its cofactor, this system may have some important role in ageing and development. The influence of age on the glyoxalase system has not been studied fully. Human erythrocytes fractionated by age have been shown to display changes in glyoxalase I (McLellan and Thornalley 1989). The present study deals with influence of age on the activity of glyoxalase I and glyoxalase II in liver, spleen and kidney of mice and rat. We have also examined the influence of ionizing radiation on age related changes on the activity of glyoxalase system.

Peroxisome proliferators constitute a novel class of non-mutagenic hepatocarcinogens. Hypolipidemic drugs which are increasingly used in therapeutic control of hyperlipidemia, plasticizers which are commonly used in industry and are ubiquitous in environment, pose potential risk to human because of their ability to induce proliferation leading to the characteristic pleiotropic response consisting of hepatomegaly, peroxisome proliferation in liver parenchymal cells and the induction of several hepatic enzymes (Lazarow and De Duve 1976, Reddy et al. 1982, Reddy and Lalwani 1983). Presently several structurally dissimilar hypolipidemic compounds and certain phthalate ester plasticizers are the two major categories of agents that are recognised as peroxisome proliferators (Reddy and Lalwani 1983). The lack of mutagenecity of these agents lead to the proposal that hepatocarcinogenesis is not related to the direct initiating effect of these chemicals (or their possible metabolites), but linked to metabolic disturbance(s) emanating from sustained increase in the number of peroxisomes in liver cells (Goel et al. 1986). Elucidation of the mechanism of induction of peroxisome proliferation and
associated enzymes by these agents is therefore considered essential in order to understand the role of peroxisomes in liver carcinogenesis induced by these drugs which do not appear to interact with and damage DNA (Butterworth et al. 1984, Gupta et al. 1985). Szent Gyorgyi (1977) proposed that methylglyoxal may change the electronic nature of protein by binding and modifying susceptible amino acid residues and thereby influencing cell division and carcinogenesis.

The modulation of the activity of the glyoxalase system by peroxisome proliferators may have great significance in evaluating and investigating the mechanism of hepatocarcinogenesis. For this purpose we have used gemfibrozil drug. We have also examined the modulation of glyoxalase system in spontaneous tumors and DEN/DMBA induced tumors.